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ORIGINAL CONTRIBUTIONS

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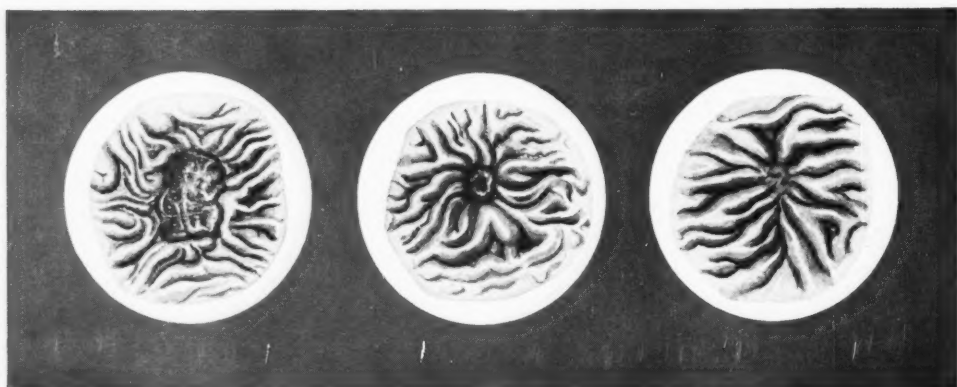
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SODIUM IN MEAT³

	Sodium Provided by 60 Gm. Serving	Sodium Provided by 100 Gm.
Beef, without bone	32 mg.	53 mg.
Lamb, without fat	66 mg.	110 mg.
Pork, without fat	35 mg.	58 mg.

Table I

SODIUM IN HOSPITAL DIETS⁴

Sodium-Poor Diets*				Very-Low-Sodium Diet†
40 Gm. Protein	70 Gm. Protein	100 Gm. Protein	130 Gm. Protein	70 Gm. Protein
400 mg. Na	500 mg. Na	800 mg. Na	1,000 mg. Na	200 mg. Na

Table II

*Foods prepared and served without salt.

†Weighed diet. May contain 4 oz. of unsalted meat.

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1. Wheeler, E. O.; Bridges, W. C., and White, P. D.: Diet Low in Salt (Sodium) in Congestive Heart Failure, J.A.M.A. 133:16 (Jan. 4) 1947.

2. Wohl, M. G., and Schneiders, N. G.: Dietotherapy (Cardiovascular Disease), in Jolliffe, N.; Tisdall, F. F., and Cannon, P. R.: Clinical Nutrition, New York, Paul B. Hoeber, Inc., 1950, chap. 27.

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4. Mayo Clinic Diet Manual, Philadelphia, W. B. Saunders Company, 1949, p. 113.

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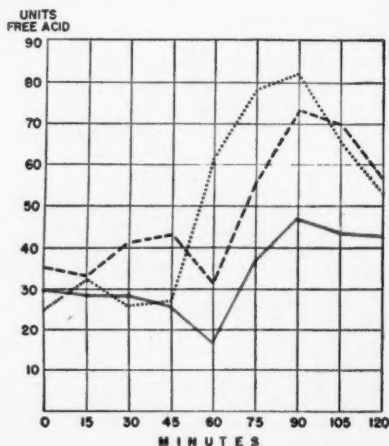
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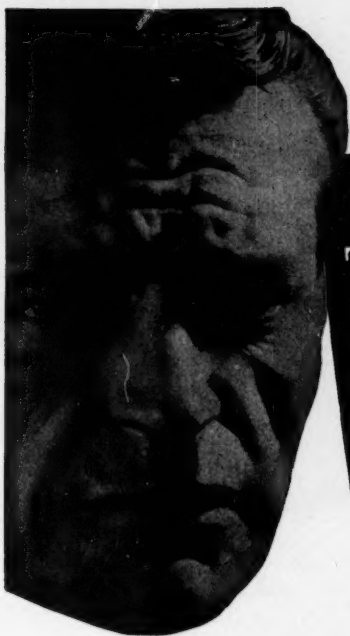
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THE INADEQUACY OF ROUTINE BARIUM ENEMA FOR THE ROENTGENOLOGIC EXAMINATION OF THE RECTUM

GEORGE LEVENE, M. D., LT. COL. NORMAN C. VEALE, M. C., Boston, Mass.

THE ROENTGENOLOGIST is frequently the first consultant called upon to determine or confirm the presence of a rectal lesion. While the rectum is the most accessible part of the alimentary tract, it is the most neglected in roentgenological examination. It is a serious condemnation of roentgenological procedure when carcinoma of the rectum is not recognized until it has produced obstructive symptoms. It is hardly surprising, therefore, to find in the literature such statements as, "Caudad to the mid-sigmoid, not only are they (x-ray studies) of limited value but they are often misleading" (1). Again, "For lesions of the rectum itself, x-ray examination is of very little value" (2).

The large amount of barium suspension introduced into the rectum by the usual barium enema will, in itself, obscure a lesion of considerable size. Moreover, superimposition of the barium-filled sigmoid may also mask a tumor of the rectum. Obviously, one useful expedient is to take films before and after evacuation of an enema in the lateral, as well as in the usual postero-anterior position, a procedure which, unfortunately, is too rarely employed. Not infrequently, the lateral film will show a lesion of the rectum that cannot be visualized on the postero-anterior films (Fig. 1).

Lateral films of the colon and rectum before and after evacuation of a barium enema are also extremely useful in detecting the presence and extent of disease in the pelvis. As has been shown elsewhere (3), the rectum and sigmoid rise up out of the pelvis and lie close to the sacrum and spine when they are distended with barium suspension or with air, and these loops fall away from the spine when they are emptied (Fig. 2). Failure of these segments to move is an indication of disease. Thus, the rectum and sigmoid may be fixed because of a carcinoma which has broken through the bowel and invaded the pelvis (Fig. 3); or they may be fixed by adhesions resulting from previous surgery, or diverticulitis, or they may be immobilized by a mass arising in the anterior pelvis or the presacral region. We are at present engaged in a study of the clinical significance of benign pelvic adhesions. This condition is most often "shrugged off" as an inevitable consequence of pelvic surgery or pelvic inflammatory disease, and usually given no further consideration. We are becoming more and more impressed with the importance of adhesions in producing significantly disturbing clinical symptoms.

For a more detailed study of the rectum, or for the demonstration of pathologic changes which, though macroscopically minute, may be very important to the patient, routine barium enema is totally inadequate. For such study we have devised a new technic (4), which consists of spraying a thin mist of barium-water suspension on the mucosa of the rectum and sigmoid. The interior of these structures is rendered visible in

their true physiologic state. There is no undue distention and the mucosa is not flattened out or obscured by a large mass of barium.

The rectum has the largest caliber of the large intestine. It begins opposite the third sacral vertebra as a continuation of the sigmoid colon, and extends to the pelvic diaphragm, where it joins the anal canal. The rectosigmoid junction is slightly constricted due to the presence of a rudimentary sphincter (the sphincter of O'Bierne). As seen from the front, the rectum presents two lateral inflexions. As seen from the side, it is flexed upon itself, conforming to the hollow of the sacrum. The rectum is divided anatomically and physiologically into an upper and lower ampulla. The mucosa of the upper ampulla is smooth, but is raised up in three semilunar folds having a supporting stroma of muscle and fibroareolar tissue. These are the valves of Houston (Fig. 4), the lowest of which is the dividing line between the upper and lower ampullae. The mucosa of the lower ampulla is gathered in longitudinal folds, the columns of Morgagni (Fig. 5) which converge to meet the smaller lumen of the anal canal. In so doing, they form small recesses (the crypts of Morgagni). The anal canal is described as varying from 2.5 to 5 cm. in length, though as seen roentgenologically, it is usually 5 cm. or more. It is lined with stratified squamous epithelium which normally is gathered into two or three delicate longitudinal folds (Fig. 6).

The fact that the rectum may be examined by other methods does not obviate the need for refinement of roentgenologic technic.

Internal hemorrhoids not infrequently escape detection by the examining finger or the anoscope since they may readily be compressed when the examining finger or anoscope is introduced. With our technic of examining the lower bowel, spraying is continued until the tip of the spraying apparatus is entirely withdrawn. In this manner, the anal canal is rendered visible. In the presence of hemorrhoids, the mucosal folds are widened, distorted and displaced, simulating the appearance of varices of the esophagus (Fig. 6).

Stercoral ulcerations (Fig. 7) are most likely to escape detection by routine barium enema and when located on the superior surface of a valve, they may be overlooked on proctoscopic examination.

Double-contrast enemas are usually employed in an effort to demonstrate polyps. Our own experience, like that of many other roentgenologists, has shown how difficult it is, at times, to differentiate a polyp from an air-bubble or other artefact.

Illustrations 8 and 9 show a case in which a routine barium enema and double-contrast enema failed to disclose a recognizable lesion of the rectum. A "spray" examination showed a polyp on the left wall of the lower rectal ampulla. As a matter of academic interest, and to confirm the reliability of the method in finding small rectal lesions, the examination was repeated one

From the Departments of Radiology, Massachusetts Memorial Hospitals, and Boston University School of Medicine.
Submitted Dec. 5, 1950.

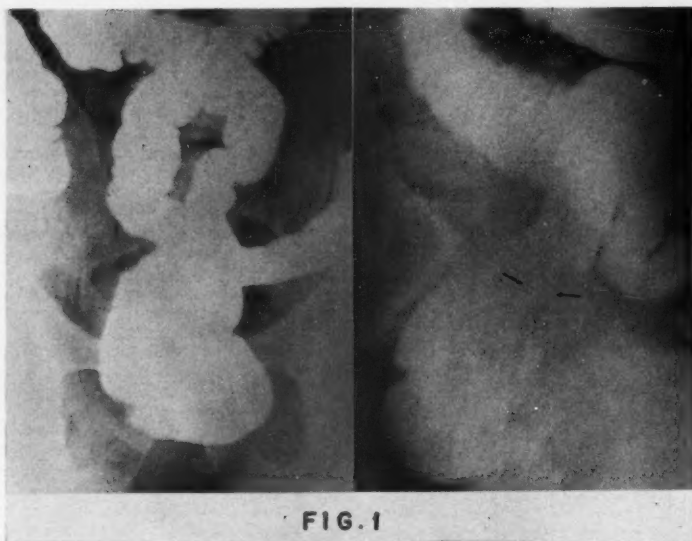
**FIG. 1**

Fig. 1. Films taken after administration of routine barium enema. The postero-anterior film fails to show the large annular carcinoma of the sigmoid which is revealed on the lateral film.

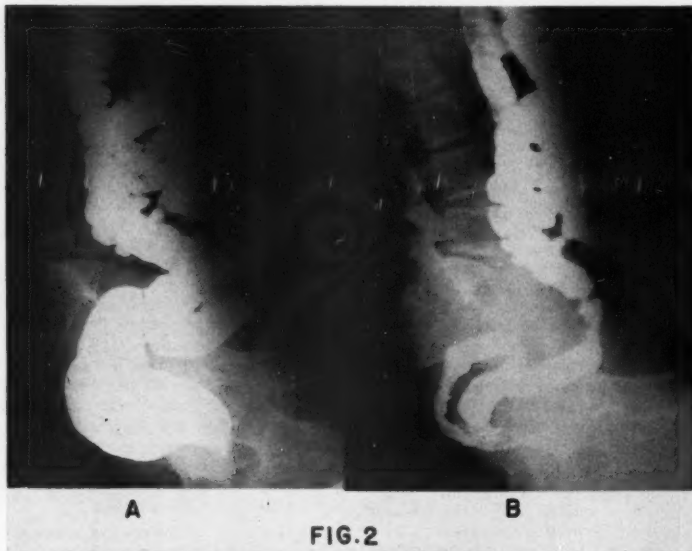
**FIG. 2**

Fig. 2. When the colon is distended with barium suspension or with air, the normal rectum and sigmoid move toward the spine and rise in the pelvis. After evacuation, these segments fall away from the spine.

A: Film taken with colon distended
B: Film taken after evacuation

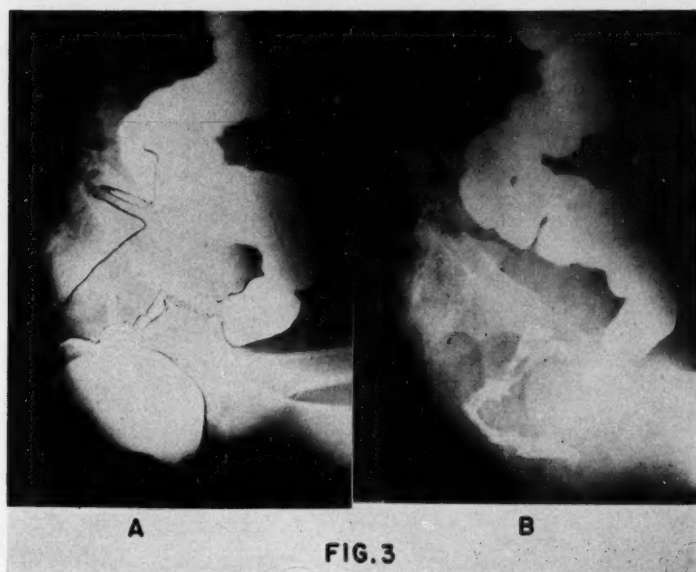


Fig. 3. Films taken A: Before and B: After evacuation of barium enema. The rectosigmoid is fixed by carcinoma which has broken through the bowel and invaded the pelvis.

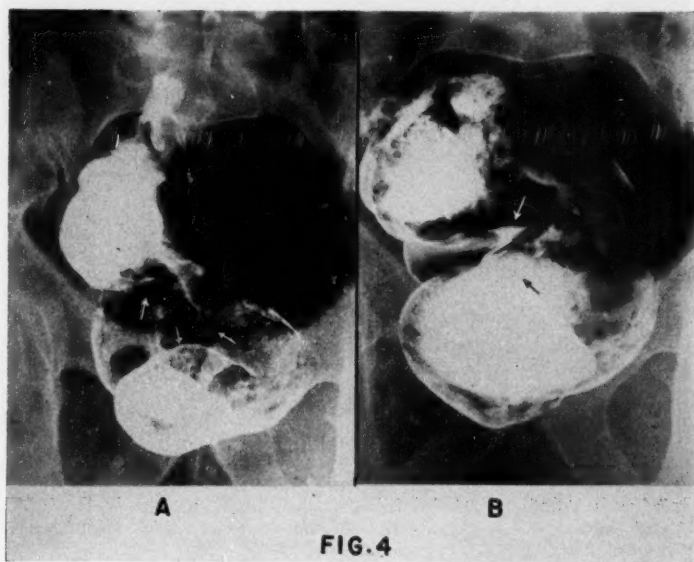


Fig. 4. Houston's valves. A: Open; B: Closed. These valves divide the rectum into an upper and lower ampulla.

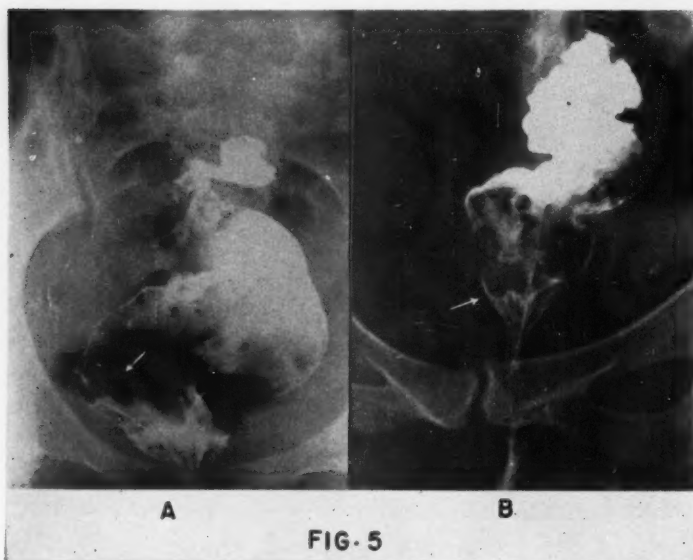


Fig. 5. A: The mucosa of the lower rectal ampulla is gathered in longitudinal folds—the columns of Morgagni.

B: Small pocket-like recesses are formed in the depths of the folds—the crypts of Morgagni.



Fig. 6. A: The normal anal canal presents two or three delicate parallel lines of "mucosal" folds.

B: Internal hemorrhoids produce widening, irregularity and displacement of the folds.

C: Prolapse of the rectum. The markings of the rectal mucosa are irregularly superimposed on those of the anal canal.



FIG. 7

Fig. 7. An area of ulceration on the superior surface of the upper valve of Houston. The valves are indurated and rigid due to chronic proctitis.

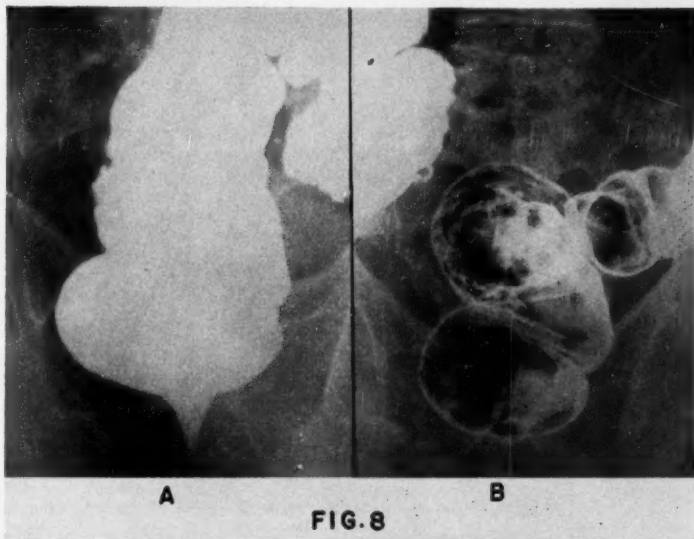


FIG. 8

Fig. 8. A: Film taken after routine barium enema. No lesion in the rectum is visualized. B: "Double-contrast" enema in the same case. No lesion can be identified. (Compare with Fig. 9.)

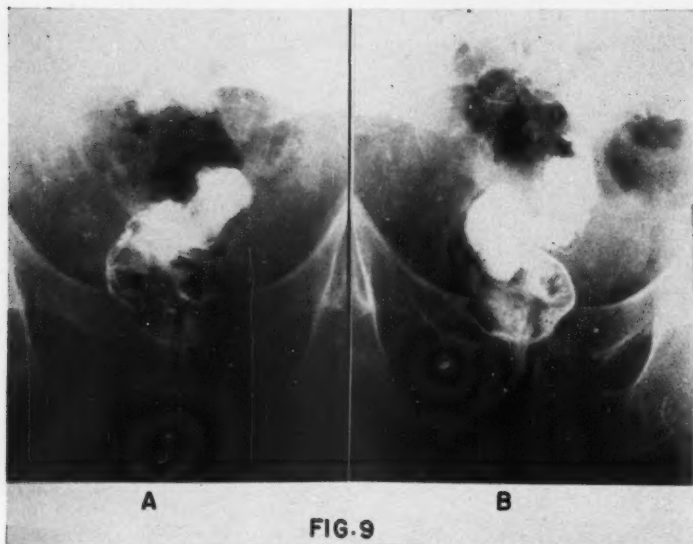


Fig. 9. A: Film of same patient as in Fig. 8, taken after examination by "spray" technic. A polyp in the lower rectal ampulla is clearly demonstrated.

B: Repeat examination of same patient by "spray" technic one week later to confirm constancy of findings—the polyp is again clearly shown.

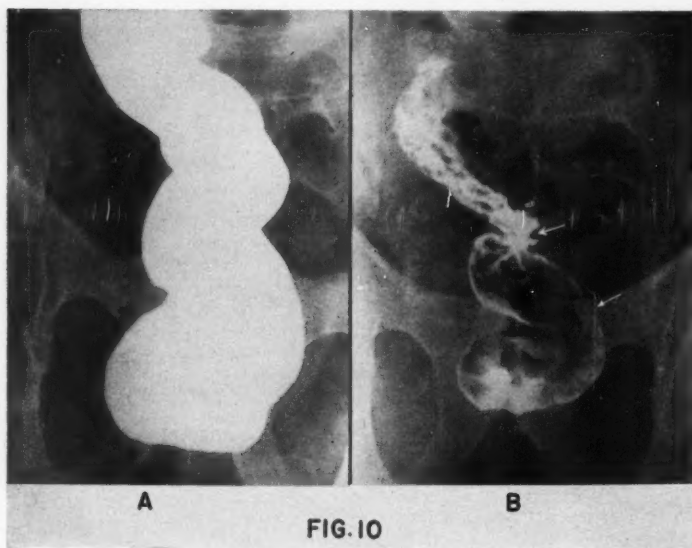


Fig. 10. A: Film taken after routine barium enema. No lesion of the rectum can be definitely visualized.

B: Film of same patient after examination by "spray technic—shows a sessile polyp (lower arrow). The sphincter of O'Bierne (upper arrow) is also well shown.

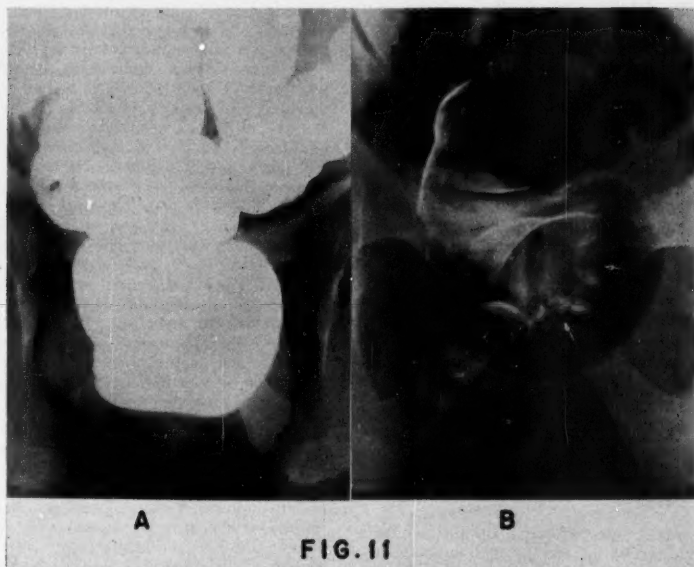


Fig 11. A: Film taken after routine barium enema. No lesion of the rectum is demonstrated.

B: Film of same patient taken after examination by "spray" technic, shows a large cauliflower mass (arrows) which occupied three-fifths of the rectal circumference. The uninvolved rectal wall is outlined by gas.

week later. An almost identical demonstration of the polyp was obtained.

Experience has shown that a routine barium enema does not lend itself to the detection of small rectal lesions (Fig. 10) and it is often equally disappointing in its failure to demonstrate large tumors of the rectum. Fig 11 shows the rectum of a patient examined with a routine barium enema, and the same case after examination with the "spray" technic. The latter reveals a mass occupying three fifths of the circumference of the rectum.

A "negative" report after examination of the rectum with a routine barium enema is not conclusive; it may, in fact, be misleading. The practice of taking films after administering a barium enema without fluoroscopic control must be thoroughly condemned. It is well known that sixty-five percent of the cancers of the large intestine are found in the rectum—a fact which

imposes a grave responsibility on the roentgenologist who submits a "negative" report in a case of rectal bleeding. It is hoped that sufficient interest may be aroused to stimulate development of newer and better methods of roentgenologic examination.

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THE ENLARGED LIVER IN DIABETES MELLITUS: ITS DETERMINATION BY PERCUSSION

JOSEPH I. GOODMAN, M. D., Cleveland, Ohio.

IN A THOROUGH review of the literature Connor (1) found that enlargement of the liver in diabetic patients, especially adults, has been mentioned only casually (e. g. 2,3). There are some references to hepatomegaly in juvenile diabetics (4-7), though it seems

paradoxical that most of the clinical reports on hepatomegaly in diabetes should be confined to the younger group. The question can be raised: Why is liver enlargement not reported more frequently in the adult diabetic?

As a rule, the liver size is estimated by palpation of the lower edge supplemented occasionally by percussion of the upper border of the hepatic dullness. Palpation of the liver frequently proves to be unsatisfactory, more so in the obese individual in whom palpation is virtually impossible. The detection of moderate degrees of enlargement of the liver presents certain difficulties in adults which are not usually present in children in whom the liver is more readily palpable because of a thin abdominal wall. Witts (8) emphasizes the fact that "the determination of the size of the liver is a more difficult feat than many people have realized." In a former study, (9) it was shown that many of the difficulties encountered in trying to evaluate the size of the livers by palpation can be resolved by the use of percussion. The practicability of evaluating the size of the liver by percussion of both the upper and lower borders was demonstrated in a series of patients with acute infectious hepatitis. In that group, many patients in whom the lower border of the liver defied palpation were shown by percussion to have enlarged livers.

PERCUSSION OF THE AREA OF LIVER DULLNESS

The upper and lower borders of hepatic dullness are delineated by percussion with the patient in the supine position. The upper border of the liver dullness coincides with the lower border of the lung and can be outlined either by direct or indirect percussion proceeding from above downward. The lower border of the liver dullness is outlined by a heavier stroke, employing as a rule indirect percussion proceeding in the direction of the costal margin from below. The distance between the upper and lower limits of dullness is measured in the midclavicular line with a tape. Should the tympany of the transverse colon or the hepatic flexure be superimposed on the liver, the point at which the percussion note becomes *absolutely flat* is taken for the measurement.

Occasionally the inferior border of the liver may be palpated in a position somewhat lower than indicated by percussion. It should be pointed out, however, that the liver edge is usually examined during deep inspiration and may descend several centimeters. On the other hand, percussion of the liver is ordinarily carried out without any special respiratory effort on the part of the patient; the position of the diaphragm is therefore but slightly altered. Failure to take into consideration the fact that the upper border likewise descends during deep inspiration can lead to large discrepancies between the two methods of examination. In our studies, the size of the liver has been based entirely upon measurements obtained by percussion of both the upper and lower borders of dullness.

The measurements obtained in this manner do not represent the actual dimensions of the liver *in situ*, but rather are an *index of the area of liver dullness*, which increases or decreases as the volume of the liver becomes greater or smaller. Incidentally, measurements obtained in cases where palpation of the lower edge of the liver is combined with percussion of the upper border are greater than the figures presented herein which are based solely on percussion of the upper and lower borders of liver dullness during quiet respiration.

In the course of the present study, it was found that the position of the liver is subject to striking variations

influenced principally by the body build. In stocky individuals and in obese persons, the liver is frequently located well above the costal margin, a so-called high lying liver. In such individuals, considerable enlargement of the liver must take place before the lower edge would become palpable; moreover, liver enlargement can extend upward even more than downward. Because of the inaccessibility of high lying livers to palpation, it is obvious that percussion has to be resorted to in cases of this sort if any enlargement is to be detected at all. The same principles apply to patients in whom the diaphragm is pushed up by increased intraabdominal pressure as a result of ascites, tympanites, etc.

In asthenic persons, on the other hand, the liver usually lies below the costal margin and errors may be made in the opposite direction, that is, a palpable liver is mistaken for liver enlargement. Such errors are avoided either by employing percussion of the upper border in conjunction with palpation or, preferably, by percussion of both the upper and lower borders of liver dullness as presented herein.

Normal liver measurements.—In order to test our method of percussion, measurements of liver dullness were taken in 86 normal adults, 57 males and 29 females (Tables 1 and 2). The average distance between the upper and lower borders of dullness obtained by percussion was 6.46 centimeters in males with lower and upper limits 5.0 to 7.8 centimeters respectively. In 29 normal women, the average measurement was 5.94 centimeters ranging from 5.0 to 7.2 centimeters. We consider a measurement above 7.5 centimeters in the male and 7.0 centimeters in the female as indicative of liver enlargement.

Liver measurements in diabetic patients.—The size of the liver was measured by the percussion technique in 101 diabetic patients at their first examination. There were 78 males and 23 females, the disproportion in the sexes being due to the fact that a large proportion of the males were patients in a Veterans Administration (Crile) Hospital. A definite increase of the hepatic dullness was found in 45 cases (44.5 per cent of the total). Of 78 males examined, 35 (including 2 children) showed an increase in liver measurements. Of 23 females examined, 10 had increased measurements.

For the purpose of analysis, the patients in this study were subdivided into 4 groups: 1. Acidosis and poorly regulated diabetes; 2. Dietary deficiency; 3. Obesity; 4. Well regulated diabetes.

1. *Acidosis and poorly regulated diabetes.*—The largest livers in the entire series were found in the cases of acidosis in males (4 cases, Table 1), with an average measurement for the group of 10.8 centimeters. There were 17 patients, 11 males and 6 females, who had been either untreated or inadequately regulated at the time the measurements were made; their average liver measurement was 9.4 centimeters for the males and 7.04 centimeters for the females. With treatment, the size of the liver decreased fairly rapidly to normal. Four patients in this group (males) were observed carefully with frequent measurements until their discharge from the hospital, at which time the area of liver dullness averaged 6.4 centimeters (normal—6.46 centimeters). One of the female patients showed a reduction in the size of the liver from 9.5 to 6.5 centimeters at the time of discharge. It appears that liver enlargement in uncontrolled diabetes is not a transient phenomenon as

TABLE I
MEASUREMENTS OF LIVER DULLNESS BY PERCUSSION IN MALES

Type of Disorder	Number of Cases	Area of Liver Dullness (Average)
Normal	57	6.46 cm. (range 5.0 to 7.8 cm.)
Diabetics	78	Enlarged liver—35
Acidosis	4	10.8 cm.
Marked dietary deficiency	8	10.6 cm. One patient with adequate diet and control of diabetes, liver dullness dropped from 13.5 cm. to 6.0 cm.
Previously untreated or poorly controlled (After 7 days treatment) (On discharge from hospital)	11 (2)	9.4 cm. (9.0 cm. (6.4 cm. (av.)
Obesity—severe	5	8.4 cm.
Obesity—moderate	15	7.67 cm. Two of these were followed and become smaller with treatment.
Child, age 10, diabetes poorly controlled	1	7.5 cm.
Child, age 8, diabetes well controlled; diet inadequate	1	11.25 cm. After 3 months on diet—6.2 cm.
Renal glycosuria	1	7.2 cm.
Emotional glycosuria	1	7.2 cm.
Mild diabetes (alimentary glycosuria).	12	6.34 cm. Includes a case of hyperthyroidism, liver measurement 6.0 cm.
Well controlled; some having insulin reactions	18	6.05 cm.
Percussion unsatisfactory due to pneumoperitoneum	1	
TOTAL 78		

TABLE II
MEASUREMENTS OF LIVER DULLNESS BY PERCUSSION IN FEMALES

Type of Disorder	Number of Cases	Size of Liver Dullness (Average)
Normal	29	5.94 (range 5.0 cm. to 7.2 cm.)
Diabetics	23	Enlarged liver—10
Marked nutritional deficiency	3	10.7 cm. After treatment: 5.9 cm. (av.)
Obesity—severe	2	10.55 cm.
Poor control of diabetes	6	7.04 cm. Liver of 1 patient dropped from 9.5 cm. to 6.5 cm. with good control of diabetes.
Obesity—moderate	8	6.94 cm.
Diabetes—well controlled	3	6.16 cm.
Child, age 10, poorly controlled	1	5.5 cm.
TOTAL 23		

illustrated by two male patients in whom the hepatomegaly persisted after 7 days of treatment in the hospital, at which time the measurements were still 9.0 and 9.8 centimeters respectively.

2. *Dietary deficiency.*—From the information in their dietary histories a marked deficiency in the food intake was found in 8 males and 3 females. The average liver measurement for the males of this group was 10.6 centimeters (Table 1) and for the females 10.7 centimeters (Table 2). In one of the males followed carefully for several months, the liver dullness actually decreased from 13.5 to 6.0 centimeters on an adequate dietary regimen. Of course the diabetes was regulated at the same time which may have influenced the rate of reduction of the liver size. One of the female patients who was followed throughout a long period of adequate dietary control had, at the time of discharge, a decrease in liver measurements from 10.0 to 5.9 centimeters.

3. *Obesity.*—The question might properly be raised as to whether obesity *per se*, that is, as a metabolic entity, exerts any effect on the size of the liver. There were 20 obese males in the present series 5 of whom weighed 200 or more pounds. The average liver measurement in the 5 excessively overweight patients was 8.4 centimeters (Table 1). The average measurement obtained in the remaining 15 moderately obese individuals was 7.67 centimeters compared with the normal of 6.46 centimeters. The average liver measurement in the 2 extremely obese female patients was 10.55 centimeters and in 8 moderately obese female patients 6.94 centimeters as compared with the average normal of 5.94 centimeters. Some of the obese patients had normal liver measurements which lowered the group average significantly. Yet many of the patients had measurements of sufficient magnitude as to leave little doubt that their livers were enlarged. At this point it ought to be emphasized that the delineation of the liver dullness by percussion is surprisingly practical in overweight persons. In only one case was it impossible to carry out percussion on account of undue thickness of the abdominal and thoracic walls. Of course, in most of these cases, palpation of the liver would prove to be futile.

4. *Well-regulated diabetes.*—There were 21 patients in whom the disease was under satisfactory control at the time of the first examination. Of these, 18 were males with an average liver measurement of 6.05 centimeters; in 3 well regulated female patients, the average was 6.16 centimeters, well within the normal range in both groups.

COMMENT

One has good reason to anticipate the existence of an enlarged, fatty liver at certain times in the course of diabetes mellitus. If this is true, the lack of emphasis in the literature on this subject is difficult to explain. From the present study, it appears that enlargement of the liver is a very frequent occurrence in diabetic patients, 44.5 per cent of the cases. Sherrill and coworkers (10) are among the few authors who stress a high incidence of associated liver disease and fatty infiltration in diabetes mellitus. Of course, the frequency of cholelithiasis and cholecystitis in diabetic patients is well known. In this series, however, insofar as could be ascertained from the clinical course, no case of outspoken hepatic disease was encountered. As regards the fatty liver

in diabetes Burns (11) clearly states that the deposition of fat in the liver is influenced by: 1. diet or starvation; 2. insulin deficiency; and 3. lack of the lipotropic substances, i.e. methionine, choline, inositol. This author recognizes the fatty state of the liver in untreated and poorly controlled diabetic patients, which, in turn, results in impaired carbohydrate metabolism and glycogen storage. If the incidence of hepatomegaly were actually as low as indicated by the literature one might be inclined, at first thought, to attribute this to the development of improved methods of treatment. Still, one cannot gainsay the fact that many cases of acidosis, newly discovered diabetes, malnutrition, etc., are encountered in which *a priori* the existence of a fatty liver must be anticipated. The detection of liver enlargement in 45 of 101 of our patients, we feel, is more in line with the expected incidence.

In our group of 45 diabetic patients in whom hepatomegaly was found, there were 21 cases of poorly regulated diabetes or acidosis. It is generally accepted that the liver in such cases is largely depleted of glycogen which is replaced by lipids mobilized from the fat depots (12-14). One of the best means to produce fatty livers experimentally is to depancreatize an obese dog or cat. In such animals, the depot fat is rapidly dissipated and the liver becomes large and fatty. Conversely Best has shown that insulin decreases the fat content of the liver of the diabetic dog.

It follows that some degree of impairment of function is likely to be present in a fatty liver (15,16). In a recent study by Brown (17) very little derangement of liver function could be detected by the usual liver function tests. Still even this author found the liver to be enlarged in some patients by physical examination, although explanation of this enlargement was not touched upon. It is generally agreed that the failure to demonstrate actual liver damage by means of the usual liver function tests does not eliminate the possibility of liver damage. The liver has great reserves and much damage has to occur before the liver function tests are significant. In the enlarged, fatty liver under discussion in this paper, it is entirely probable that the individual fat laden liver cells are not 100 per cent normal, but sufficiently so that the amount of impairment would not alter the function tests.

Labbe, Boulin and Balmus (18) reported four cases of acidosis in which enlargement of the liver and fatty infiltration of the parenchymal cells was a constant finding at autopsy. The occurrence of markedly enlarged livers in our 4 patients (and in many cases not included in this series) with acidosis strongly supports this data. It was gratifying to find in our patients that one can follow the fluctuations in liver size during acidosis by taking repeated measurements of the area of liver dullness.

In 11 patients with malnutrition and diabetes, hepatomegaly appeared to develop principally as a consequence of lipotropic deficiency (choline, methionine, or vitamin lack), a condition which obviously can occur just as readily in non-diabetic individuals. In fact, some of the largest livers of the entire series occurred in this group (see Tables 1 and 2). Although malnutrition was of prime importance in these patients, we cannot agree with Biskind et al (19) that it is the principal factor in the production of hepatomegaly in diabetes or that the pathologic liver thus

produced is the main factor in the etiology of diabetes mellitus.

The remaining 13 patients with hepatomegaly were overweight diabetics of the mild type in whom the liver is prone to be infiltrated with lipids (20-22). If it is permissible to draw conclusions from the size of the liver in diabetic patients, one can state that obesity may produce moderate degrees of hepatomegaly, whereas in the case of marked obesity there is undeniably evidence of significant liver enlargement. It should be stressed that in obese individuals with a thick panniculus adiposus an enlarged liver might readily be missed by palpation. Yet with the use of percussion, liver enlargement was a common finding in this obese group—13 out of 30 cases.

The detection of alterations in the size of the liver in diabetes also has some therapeutic value. The institution of insulin in cases of poorly regulated diabetes and acidosis and of an appropriate diet in cases of malnutrition are clearly indicated. However, the same approach certainly is not indicated in the obese diabetic individual. This type of patient ordinarily consumes a well-balanced diet and the diabetes is mild. As in the case of the other organs, the liver of an obese individual may assume the function of a fat depot. It seems to us that the prevention and the treatment of hepatomegaly in the obese diabetic individual is directly dependent upon loss of body weight. The prescription of a weight reduction regime is necessary and, we believe, gives an excellent prognosis for the disappearance of the hepatomegaly. Unfortunately, because of the length of time involved, it is not always possible to observe the response of the liver in overweight patients on a reducing diet under hospital conditions. We were fortunate to have had the opportunity to observe two of the male patients in the hospital for a sufficiently long period to be certain that the liver had diminished significantly in size following a loss in weight.

SUMMARY

1. The physical diagnosis of the livers and the advantages of percussion as compared with palpation are presented.
2. In many patients, particularly in obese individuals with high lying livers, percussion is the sole means of estimating liver size.
3. By means of percussion of the area of liver dullness, hepatomegaly was detected in 44.5 per cent of 101 unselected diabetic patients.
4. In the group of 45 cases with liver enlargement, 21 had *insulin deficiency* as evidenced by poorly regulated diabetes or acidosis; 11 patients had *lipotropic deficiency* as determined from the dietary history; the remaining 13 patients were *obese* mild diabetics.

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CAROTINEMIA AND HEPATIC DYSFUNCTION IN DIABETES MELLITUS

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THE CAROTINEMIA (5,14,16,21,22,31,32) and the hepatic disorders (3,4,6,7,10,19,20,26,30) associated with diabetes mellitus have been separately observed with varying, yet generally comparable frequency. That this aberrant pigment metabolism may reflect a disturbed liver function has long been considered a possibility and is consistent with even the newer concept of carotene-vitamin A transformation in the intestinal wall (35).

Since the simultaneous determination of carotene concentration and liver function in diabetes might demonstrate at least a suggestive parallelism, a study was undertaken in a group of outpatients. Blood serum levels of carotene, vitamin A, cholesterol and bilirubin were determined, and the cephalin flocculation and thymol turbidity tests were performed in each instance. In addition, patients were examined for hepatomegaly, splenomegaly, neuropathy and clinical signs associated with impaired liver function.

MATERIAL AND METHODS

Sixty-five (13 male and 52 female) patients from the diabetes clinic were studied on a non-selective (consecutive cases) basis. Blood specimens were drawn in the post-absorptive state before the administration of the day's insulin. Physical examinations were conducted separately (on all but 5 patients) during routine clinic visits.

Carotene and vitamin A determinations on serum (in a few instances, on plasma) were performed by the method of Kimble (15), employing the Carr-Price reaction. The serum cholesterol was determined by Bloor's method (1). The serum bilirubin was measured by the method of Malloy and Evelyn (18), and the cephalin flocculation and thymol turbidity by the methods of Hanger (9) and Maclagen (17) respectively.

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RESULTS

Results are outlined in the accompanying table.

Normal values as determined in this laboratory are accepted as: serum carotene, 80-300 micrograms per cent; serum vitamin A, 30-100 micrograms per cent; vitamin A carotene ratio, above 0.2; serum cholesterol, 150-200 milligrams per cent; total serum bilirubin, less than 0.7 milligrams per cent; cephalin flocculation, less than 3 plus; thymol turbidity less than 5 units.

Of the 65 patients, 7 (11%) showed a serum carotene level of 300 micrograms per cent or more ("carotinemia"), and another 22 (34%) had levels of 200 or over (a relatively high normal range). Three patients (5%) showed vitamin A levels below 30 micrograms per cent; none of these had excessive carotene concentrations. Seventeen patients (26%) had vitamin A-carotene ratios of less than 0.2, of whom all but 2 had serum carotene levels above 200 micrograms per cent. Fifteen patients (23%) exhibited an elevated serum cholesterol level, and 6 of these had carotene concentrations over 200 micrograms per cent. Bilirubin concentrations were normal in every instance. The cephalin flocculation test was abnormal in 3 cases (5%), and the thymol turbidity in 5 individuals (8%).

Of the 60 patients on whom physical examinations were conducted 30 (50%) had a palpable liver, 10 (17%) had evidence of neuropathy (4 of these with a palpable liver) and one had a palpable spleen (without a palpable liver).

Three of the 7 patients with carotene levels over 300 micrograms per cent had a palpable liver, and 12 of 28 examined with levels above 200 had a palpable liver. One of 2 patients examined with vitamin A levels below 30 micrograms per cent had a palpable liver, and 9 of 16 with levels below 40 exhibited this phenomenon.

There was no apparent correlation between the presence of abnormal findings and the sex, age or race of the patient, or the duration or severity of the diabetes.

DISCUSSION

The criteria adopted in this study are necessarily

TABLE SHOWING SIGNIFICANT CLINICAL FEATURES AND LABORATORY FINDINGS OF DIABETIC PATIENTS

Number	Initials	Sex	Race	Age	Duration	Severity	Carotene Micro. Gms. Per. 100 cc.	Vit. A Micro. Gms. Per. 100 cc.	A/Car. Ratio	Cholesterol Mgms. Per 100 cc.	Bilirubin Mgms. Per 100 cc.	Ceph. Flocc.	Thymol	Significant Physical Findings	Complicating Conditions
1	EM	F	W	60	*1	3	239	51	.21	212	0.3	1	3.5		
2	MB	F	W	61	6	2	176	45	.26	80	0.5	3	2.5	Liver Palpable Neuropathy	Lacune's Cirrhosis
3	VX	F	W	56	10	3	292	51	.17	138	0.4	1	3.5		
4	MB	F	W	52	2	2	271	36	.14	215	0.3	0	7.5	Liver Palpable	
5	RY	F	C	59	6	4	69	46	.67	132	0.7	2	4.0	Liver Palpable	Hypertensive Arter. Hrt. Disease Glaucoma
6	GL	F	W	38	4	4	222	62	.28	320	0.3	1	4.0		
7	VN	M	W	71	1	3	394	53	.13	215	0.2	0	1.5	Liver Palpable Neuropathy	
8	JS	F	W	55	*1	2	148	39	.26	260	0.3	0	2.5	Liver Palpable	
9	AP	F	W	50	8	3	162	25	.15	160	0.2	1	7.0		Hypertensive Cardiovascular
10	RD	F	W	36	4	3	176	36	.20	223	0.3	0	2.5		
11	DC	F	C	43	11	4	107	109	1.0	132	0.4	2	4.0	Neuropathy	Hyper. & Art. Hrt. Disease Anemia
12	HS	F	W	25	13	4	183	59	.32	240	0.4	0	1.0	Liver Palpable	
13	PG	F	W	41	3	3	170	31	.18	168	0.6	2	25	Liver Palpable	
14	MD	F	W	55	3	2	402	51	.13	260	0.3	0	1.5		
15	DP	F	C	52	15	2	102	33	.32	143	0.4	0	3.5		
16	MG	F	C	31	7	3	246	49	0.2	260	0.3	0	1.5		
17	JS	F	W	52	10+	4	129	43	.33	240	0.2	0	2.2	Neuropathy	Lactic & Art. Hrt. Disease
18	FN	F	W	59	1	3	98	29	.30	175	0.7	0	2.5	Liver Palpable	Gall Blad. Disease Rheum. Arthritis
19	BS	M	W	60	*1	4	220	189	.29	198	0.3	0	2.5	Neuropathy	Arter. Hrt. Disease
20	HS	M	W	64	*1	3	104	68	.65	190	0.3	1	1.0		
21	MS	F	W	63	30	3	200	57	.29	250	0.3	0	1.0	Neuropathy	Hyp. & Art. Hrt. Dia. Died Myocard. Infarction
22	AK	F	W	71	*1	2	100	43	.43	105	0.3	1	2.0	Liver Palpable	
23	AB	F	C	46	2	4	84	44	.52	210	0.4	1	5.0		
24	ME	M	W	76	12	2	140	48	.34	205	0.3	1	1.0		Art. Hrt. Disease Hydro-nephrosis
25	HL	F	W	26	6	3	66	55	.83	170	0.2	2	2.0		
26	AS	M	W	49	8	4	692	45	.07	230	0.3	0	1.5	Liver Palpable Carotid Pigment	
27	AV	F	W	56	8	4	195	98	0.50	205	0.3	0	1.5		
28	FT	F	W	70	2	2	308	36	.12	170	0.3	1	2.5	Liver Palpable	Art. Hrt. Disease
29	FS	F	W	56	15	4	258	56	.22	190	0.2	1	3.0		
30	CM	F	W	35	*1	2	214	42	.20	170	0.3	1	3.0		
31	AR	F	W	60	1	4	168	37	.22	198	0.2	2	2.0	Liver Palpable	
32	MS	F	C	54	2	2	243	38	.16	120	0.2	0	2.5	Liver Palpable	
33	AB	F	W	60	25	2	217	53	.24	215	0.3	0	2.5	Liver Palpable	Serological Lues

34	MM	F	W	65	15	4	219	30	.14	185	0.2	2	1.5	Neuropathy	Hyper. & Art. Hrt. Disease
35	MD	F	W	12	6	4	135	34	.25	198	0.3	1	1.5	Liver Palpable	
36	AJ	F	C	52	10	2	374	73	.19	170	0.3	1	3.5		Hyp. & Art. Hrt. Dis.
37	RA	F	W	74	*1	2	274	45	.16	170	0.2	1	3.5	Liver Palpable	
38	JD	M	W	62	6	3	159	83	.52	165	0.2	1	1.0	Liver Palpable	Art. Hrt. Dis. Art. Generalized Periph-eral Vas-cular Dis.
39	CB	M	W	61	2	2	258	57	.22	260	0.3	1	2.5		
40	AL	F	W	60	3	2	262	45	.17	305	0.3	1	1.5	Liver Palpable	
41	MB	F	C	59	4	2	173	71	.41	215	0.3	1	2.0	Liver Palpable	Art. Hrt. Dis. Hydro-Nephrosis, Nephro-lithiasis Sero. Lues Rheumatoid Arth.
42	AO	F	W	60	1	2	243	44	.18	190	0.3	1	2.5	Liver Palpable	
43	PK	F	W	60	*1	2	158	38	.24	230	0.3	1	1.5	Liver Palpable	Hyp. & Art. Hrt. Dis.
44	MO	F	W	61	16	2	59	40	.68	120	0.3	3	3.0	Liver Palpable Neuropathy	Rheumatoid Arth.
45	ML	F	W	48	1	2	258	57	.22	143	0.2	1	1.5		
46	ER	M	W	50	3	2	225	51	.23	105	0.2	3	1.0	Liver Palpable	
47	AS	M	W	63	2	2	108	46	.43	175	0.3	1	4.0	Liver Palpable	
48	VF	M	W	62	8	3	118	32	.27	143	0.2	1	1.8	Liver Palpable Neuropathy Xanthoma	
49	SD	F	W	59	4	3	162	43	.27	170	0.2	0	1.5		
50	GM	F	C	54	5	2	416	52	.13	190	0.2	3	3.0	Carotene Pigmentation	
51	RW	F	W	72	27	2	156	44	.28	160	0.3	1	3.0	Liver Palpable	Rheumatoid Arth.
52	CF	F	W	62	12	2	149	50	.34	230	0.3	1	2.5	Xanthoma	Hyp. & Art. Hrt. Dis.
53	EL	F	C	53	1	3	253	54	.21	120	0.2	1	2.0		
54	MF	F	W	56	13	3	177	46	.26	230	0.2	0	1.5		Art. & Luetic Hrt. Dis. Adeno-Ca. Rectum Resected 8 yrs. Ovarian Cyst
55	AL	F	W	71	6	2	246	38	.15	215	0.6	1	2.0		
56	CC	F	W	47	*1	2	180	58	.32	160	0.3	1	1.0	Liver Palpable	Mild Thy-rotoxicosis on propyl-thiouracil
57	BP	F	W	62	*1	2	225	56	.25	120	0.2	1	4.0	Liver Palpable	
58	SS	F	W	52	*1	2	315	50	.16	205	0.3	1	1.5	Liver Palpable	Hyp. & Art. Hrt. Dis.
59	AR	F	W	53	20	4	176	39	.22	205	0.3	1	3.5	Neuropathy	Gangrene Foot
60	MS	F	W	41	5	4	170	44	.26	170	0.4	1	1.2		Foot Infection
61	MB	F	W	43	1	2	145	36	.25	215	0.3	1	2.0		
62	SS	M	W	65	14	4	112	27	.24	80	0.2	2	5.0		Died Carci-noma of cecum, metastasizing
63	RC	F	W	65	7	2	222	57	.26	185	0.3	1	5.5		Asthma
64	OE	F	C	61	11	2	118	52	.44	170	0.2	0	2.5		
65	MC	F	W	68	20	2	181	45	.25	190	0.3	1	1.0		Hypertrophic Arth.
AVERAGE:				55	7	2.7	203	48	.24	190	0.3	1	2.5		

DURATION: Documentated Diabetes: Patients less than 1 year listed as 1 with asterisk.
SEVERITY: Mayo Clinic Classification: All patients on prescribed diet (eliminating group 1.)

arbitrary, since with respect to serum carotene and vitamin A levels, at least, reported normal values vary widely. In the experience of this laboratory, however, the figures of 300 micrograms per cent or more for carotene, and 30 micrograms per cent or less for vitamin A are outside the range normally encountered. Likewise a carotene concentration of 200 to 300 micrograms per cent and a vitamin A level of 30-40 micrograms per cent are at the extremes of average—hence suggestive of an abnormal tendency.

In this series the incidence of carotinemia is lower than in most studies recorded (5,14,16,21,22,31,32), although the ratio of vitamin A to carotene is smaller than the normal figures of Popper et al (27). Similarly the percentage of patients with liver damage is lower than in those of most diabetic groups reported (3,4,6,7,10,19,20,26,30), although other liver function tests, notably the bromsulphalein retention test might have yielded a greater number of abnormal patterns. The serum vitamin A level, itself, of course, provides some index of hepatic function.

Since, too, a palpable liver is not necessarily an enlarged (inferentially, abnormal) organ (23), any estimate of hepatic disorder based on palpability alone would undoubtedly be too high.

The reasons for the relatively low incidence of carotinemia and of liver damage are not apparent. Although there is seemingly no correlation between the intensity or duration of the diabetes process and the degree of carotinemia or hepatic dysfunction, the low incidence of hypercholesterolemia may result from generally good control of the diabetes in this series, including emphasis on the high protein content of the diet. A tendency towards a lower intake of foods high in carotene (not evaluated in this study) may likewise well be a factor. Moreover, a series of diabetics has been reported with completely normal liver function tests (2), serum carotene levels have also been noted in more recent reports, in contrast to older surveys (5,14,16,21,22,31,32).

The apparent lack of correlation between serum carotene or vitamin A concentrations and serum cholesterol levels differs from results recorded elsewhere (12,13). However, while both elevated carotene and cholesterol figures might be anticipated in poorly controlled diabetes (even with parallel changes in many instances) the mechanisms governing their concentrations in the blood are too many and too varied to permit valid interpretation of these findings.

Although the ultimate fate of ingested carotene (and vitamin A) is not known (37), carotinemia is generally (possibly wrongly) assumed to indicate an impaired mechanism of transformation of the pigment precursor into the vitamin. The close relationship of the liver to the metabolism of vitamin A is regularly demonstrated by changes such as those observed—in hepatitis (24, 34) and in cirrhosis (8,11,24,28,33,36), but any direct role for the liver in this conversion process is necessarily inferred rather than factually established. Moreover, if, as suggested by the work of Sexton et al (35) in rats, the intestinal wall is the site of conversion, the low vitamin A levels noted in liver disease may result from the abnormalities of the bowel associated with advanced hepatic dysfunction (25,29).

In this group of diabetics, at least, the apparent lack of correlation between liver damage and an excessive concentration of carotene in the blood seems most con-

sistent with the existence of an extra-hepatic site for its conversion into vitamin A.

SUMMARY AND CONCLUSIONS

Sixty-five patients with diabetes mellitus were investigated for evidence of carotinemia, lowered serum vitamin A concentration and of hepatic dysfunction.

Carotinemia was demonstrated in 11 per cent of the patients, none of whom showed an abnormally low serum vitamin A level. An elevated serum cholesterol concentration was noted in 23 per cent of the group. There was minimal laboratory evidence of liver disease, although 50 per cent of 60 patients examined showed a palpable liver.

There was no correlation between carotinemia or decreased serum vitamin A levels and evident liver damage, nor between any of these findings and the age, sex or race of the patients or the severity or duration of the diabetes.

If carotinemia in diabetes does indicate impaired conversion of the pigment into vitamin A, the results of this study seem more compatible with the existence of an extra-hepatic rather than a hepatic site for this mechanism.

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DIABETIC CASE FINDING—A NEW TECHNIQUE

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DIABETIC CASE FINDING has now taken its place with tuberculosis case finding. The nationwide urban Diabetes Detection Drives, sponsored by the American Diabetes Association, and the United States Public Health Service multi-screening health projects, prove the point. Case finding depends on urinalysis as the initial step. From experience gained in diabetes detection work, one rapidly comes to the conclusion that *any means* to facilitate the obtaining of a large number of urine specimens in a community survey is most desirable. A new type of specimen container has recently been described (1). Its use should result in better participation in future diabetes detection drives.

Heretofore, gross urine specimens have been utilized. Where the survey reaches the populace at home, this has meant the distribution of new or washed bottles to insure sanitation and eliminate contamination by sugar from an old bottle's previous content. In some cases, no provision has been made to protect specimens from fermentation. Where a preservative has been provided, it has usually been a tablet. This has occasionally been discarded by the user, and worse, there are known cases where the user has swallowed the tablet before passing the specimen.

In St. Louis, distribution of specimen bottles without preservative was accomplished by cooperating druggists. It was necessary for the individual to obtain a bottle from his druggist and subsequently return the filled bot-

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tle to his drugstore, for relay to a central testing laboratory. (3) Aside from public inertia in going through these motions, the impression was gained that many a person was deterred by both modesty and an infringement upon his sense of aesthetics.

Another mechanism used widely also depended upon druggist cooperation. Druggists, themselves, made urine sugar analyses, sending reports to the local committee for follow-up. Personal reports from a number of cooperating druggists revealed that, in their opinion, the public is resistant to the idea of urinalyses at drugstores, because they regard drugstores as pre-eminently sanitary and they regard druggists as DRUGGISTS. This opinion of the druggists themselves no doubt limited their active cooperation. It is also pointed out that suburban and rural population segments have been unable to benefit by participation in Diabetes Detection Drives, which, of necessity, have been urban endeavors in public health.

The urine container mentioned above obviates many of the difficulties discussed, because it is easy to use by the complete novice; it is transportable in an ordinary envelope; it permanently preserves any sugar content; and it is inexpensive.

The Dreyapak* (R) container, briefly, consists of a light compressible cellophane-like outer covering (A), (see Figure 1.), filled with an absorbent core (B) containing a preservative in the dry state. The container has the approximate circumference of a cigarette, and is about two-thirds its length. The plastic cover over-

*Dreyapak (Reg. T. M.).

laps the core at both ends, and is sealed by twisting at one end. The other end is not twisted and extends beyond the core about one centimeter. Through this open end the specimen is deposited by any of several methods:

- a. By means of a medicine dropper (Fig. 1);
- b. By using an ordinary drinking straw as a finger pipette;
- c. By dipping the open end of the container into the urine, collected in any suitable vessel, deep enough so

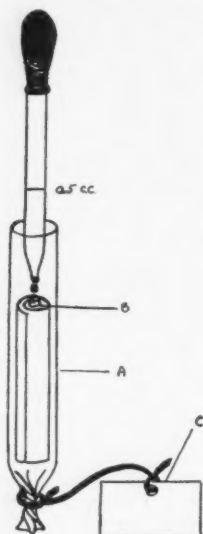


Fig. 1.

that the urine and absorbent core make momentary contact. In this case, it is necessary to prevent an air lock either by making a pin-hole opening in the plastic cover near the closed twisted end or by simply leaving both ends open until after the Dreypak (R) container has been filled. The outside of the container is wiped dry with toilet tissue or paper.

Having loaded the container by any one of these methods, the open end (or ends) are twisted shut. The container carries identifying data by attached tag (C—

Fig. 1), or it may be inserted into a small envelope on which is recorded name, date, etc. In either case, the tag or card also carries specific instructions on the method of use. In any form, the Dreypak (R) container lends itself to transport to the laboratory in an ordinary envelope. (Fig. 2).

Sugar testing may be qualitative or quantitative; where quantitative testing is done, exactly 0.5 c.c. of urine is deposited on the absorbent core. The qualitative test may be performed by any method using an aqueous reagent, which, at the same time, serves as an extractive. Upon arrival at the laboratory, the twisted ends are snipped off and discarded. The remainder, after having been slit lengthwise with a razor blade, is placed in the test tube with the reagent, and heat is applied. For qualitative and quantitative testing, we have used Somogyi's method (2) with complete satisfaction. The color reaction appropriate to the method occurs promptly.

Our preference has been to use aqueous reagents (Benedict's or Somogyi's). Clintest can be used in the following way: Two Clintest tablets are dropped in a dry test tube; the Dreypak (R) container slit open, as described above, is dropped on top of the tablets; 2 c.c. of water (thirty drops) are dropped into the tube and the reaction quickly ensues. The method is sensitive to 0.2%. If the Dreypak (r) container has been filled with exactly ten drops of urine, and if the container is completely dry at the time of testing, the above procedure will give results comparable to the standard Clintest quantitative method. (6).

Technician response to this container has been most favorable. There is no opening of urine bottles and no transfer of liquid urine to the test tube. Spilling is completely eliminated and at least two time-consuming operations in the laboratory are avoided. These considerations are of importance when many specimens are to be examined.

Although determination of albumin plays no part in diabetes detection, it may play a part in a multi-screening project. The Dreypak (R) container may be used for albumin determination by preparing the container as for the sugar tests described. 6-7 c.c. of approximately 0.1% sodium hydroxide (NaOH) are placed into the test tube with the urine container. The tube is gently agitated and filtered. The filtrate is acidified to litmus with 3% acetic acid and heated to boiling. Turbidity will develop commensurate with the amount of albumin present. When both sugar and albumin are to be tested, duplicate containers are submitted.

Diabetes detection, according to Peck, "must obviously

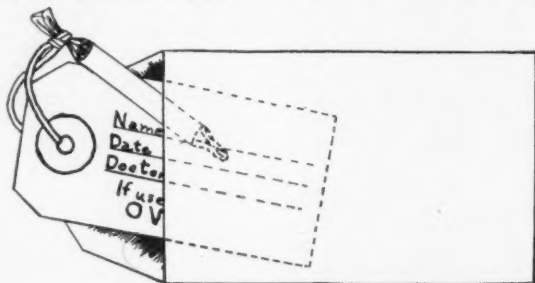


Fig. 2.

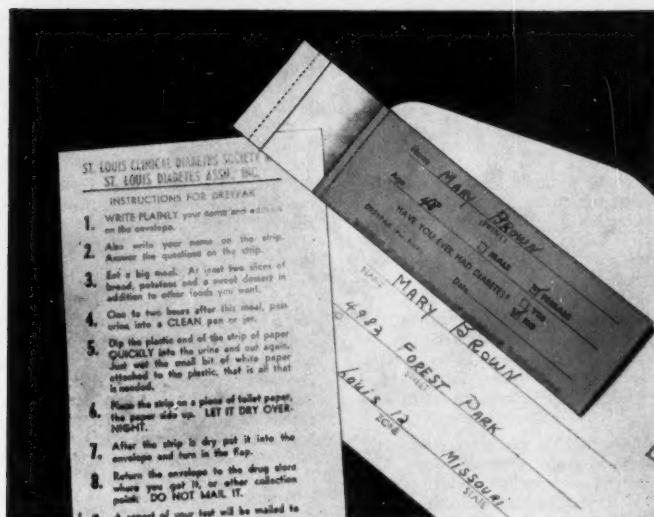


Fig. 3.

be a day-by-day, week-by-week, continuous all out endeavor." (4). The keystone of diabetes detection should be the individual physician. The golden opportunity presents itself whenever he finds a new diabetic. The tendency for diabetes to be familial is well known, but it is usually difficult to get members of a given patient's family to cooperate and submit specimens for sugar analysis. Our experience with the new container has been encouraging. We distributed twenty-six of the containers to families of three newly-discovered dia-

betics. All of them were returned for analysis. Three revealed glycosuria and two of those were subsequently proven to have diabetes. No conclusion can be drawn from such a limited experience, but we cannot refrain from pointing out this incidence of 7.7%, as compared to the 1.5% to 3% reported in surveys of the general population. (3). The results do not differ much from those quoted by White and Pincus, in a statistically significant survey of parents and siblings of diabetics. (5).

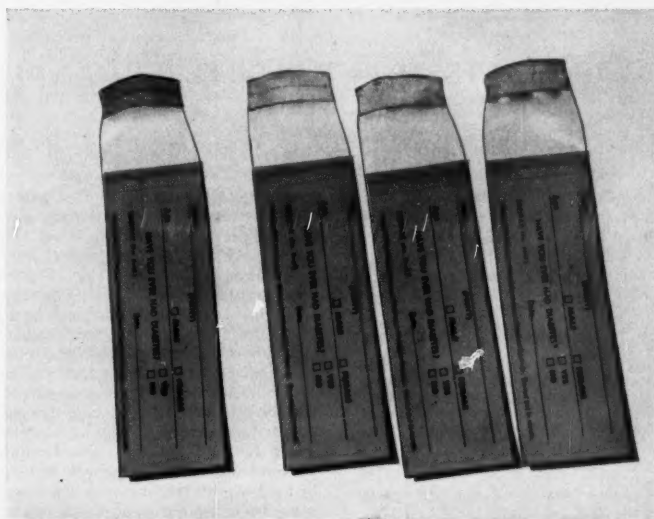


Fig. 4.

In the original report (1), we described controlled quantitative experiments with the specimen container covering a range from 1/4% to 6%. The stability was proven for periods up to two weeks. We have now repeated tests on known samples, after allowing them to remain at room temperature or higher (on radiators) for 90 days, and find the sugar content well-preserved in all concentrations. (6).

For those physicians who periodically check the glycosuria of their patients quantitatively, this method of collection and transportation greatly facilitates the follow-up examinations of diabetic patients. The patient can send his sample in an envelope the day before his appointment with his physician. This makes for more efficiency in the physician's office or the hospital laboratory, where the day's urinalyses can all be run at the same time. As for the patient, he is spared the trouble of packaging and mailing the relatively bulky bottles, or the necessity of carrying these to the doctor. He is also spared the wait while the specimens are set up and examined.

At the present time, we find the container completely satisfactory for micro-blood sugar determinations. The method will be the subject of a future report. Using finger blood samples is so simple, that collecting blood for diagnostic carbohydrate tolerance tests may become routine practice at any physician's office. Studies are also in progress for the utilization of the Dreyapak (R) container for other blood chemistry and for serologic tests.

With the cooperation of the St. Louis Clinical Diabetes Association, the Dreyapak container has been modified for mass survey use. This modification is only suitable for Qualitative testing for sugar. Dreyapak Qualitative consists of a cardboard 4 1/2 x 1 1/2 inches to which is sewed a polyethylene extension bringing the overall length to 5 1/2 inches. The free end of the polyethylene is covered with a half inch strip of prepared filter paper attached

by sewing. (See illustration No. 3). This device, with an instruction sheet, fits into an ordinary 6 1/2 x 3 3/4 inch envelope.

In use, the filter paper end is immersed momentarily in the properly collected urine and then allowed to dry. When the dried Dreyapaks reach the laboratory, twenty to thirty are held in one hand by the cardboard handle and the filter paper plastic end is immersed for one minute in boiling Benedict's (Qualitative) reagent. The reaction is prompt and the positives show various intensities of yellow, whereas the negative become slightly blue from the unreduced copper sulfate. (See illustration No. 4). Excess Glucose from a positive filter paper causes reduction of the copper salt in the solution. This precipitates quickly and prevents contamination of the negatives. Whenever much precipitate forms, it is best to change to fresh reagent. In mass surveys, where about 98% of the specimens are negative, this does not present much of a problem. The polyethylene backing each filter paper strip also helps to prevent contamination of the negatives by the positives. In our hands, two technicians can run 400 to 600 specimens in an hour. Although limited in its usefulness, this modification has the advantage of mass handling in the laboratory.

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THE FLOCCULATION TESTS IN THE DIFFERENTIAL DIAGNOSIS OF JAUNDICE

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SINCE JAUNDICE of a hemolytic nature can, as a rule, be excluded easily by clinical and laboratory methods, the difficult problem of the differential diagnosis of jaundice amounts in principle to a differentiation between medical conditions (due to various types of acute or chronic hepatitis, including cirrhosis) from surgical conditions in which an extra-hepatic biliary obstruction is produced by a calculus, tumor or stricture.

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The original approach in the laboratory diagnosis of jaundice was the demonstration of functional impairment of the liver by various tests. This was done with the idea in mind that in medical conditions liver function damage is demonstrable whereas it is absent in mechanical biliary obstruction. However, one gradually appreciated that in the surgical type of jaundice liver cell damage may also occur due either to prolonged obstruction (biliary hepatitis) or to secondary bacterial infection. Aside from the fact that few basic functions of the liver lend themselves to simple laboratory tests, the demonstration of liver cell damage as such appears then not as the sole problem in the differential diagnosis. Thus, through the years the laboratory diagnosis of jaundice became more complicated rather than simplified (1). In recent years various flocculation tests have been widely applied in hepato-biliary diseases despite the fact that none of them can be considered

TABLE I. RESULTS OF GAMMA GLOBULIN TURBIDITY AND ZINC SULFATE TURBIDITY TESTS IN HEPATO-BILIARY DISEASES

Diagnosis	No. of Cases	Gamma globulin turbidity			Zinc sulfate turbidity		
		Mean	% above 1.25 gr. %	% above 2 gr. %	Mean	% above 12.5 units	% above 20 units
Severe viral hepatitis	51	1.77	90.4	27.5	19.7	88.2	51.0
Mild viral hepatitis	27	1.44	77.7	0	15.0	70.4	22.2
Recovered viral hepatitis	33	1.49	60.7	0	16.7	75.8	21.2
Chronic viral hepatitis	18	2.14	94.5	61.2	33.6	94.5	77.8
Cholangiolitic hepatitis	5	1.25	40.0	0	10.7	40.0	0
Toxic hepatitis	44	1.52	63.6	31.8	15.6	52.3	22.7
Cirrhosis with jaundice	87	2.05	92.0	56.4	23.1	88.5	60.9
Cirrhosis without jaundice	74	1.91	89.5	44.5	20.4	73.0	51.4
Obstructive jaundice	57	1.51	75.4	8.8	10.6	26.3	8.8

in any way an hepatic function test. In practical application, however, they proved to be more useful than most of the hepatic function tests. They are simple, not time consuming and require little equipment. For their practical use, however, it is necessary to understand their physical chemical basis and even more so the pathologic significance of abnormal results. With this understanding in the following a simple system of combined use of several tests in the differential diagnosis of jaundice will be presented and illustrated by diagnostic results obtained.

The flocculation tests are based on the instability of serum colloids when serum dilutions are mixed with various reagents. A developing flocculation is arbitrarily graded or a turbidity is compared with that of standard solutions and recorded either in units or in grams per cent calibrated with serum protein. These reactions reflect alterations of the serum proteins. Many of the flocculation tests have been originally devised as a result of by-chance observations of flocculations developing with abnormal sera without understanding of their physical chemical basis. Nevertheless, the basis of most of the tests is now fairly well understood as a result of studies with rather complicated methods, such as the electrophoretic partition of the serum proteins according to Tiselius.

Among the large number of recommended tests the following four will receive special emphasis here: the gamma globulin turbidity test of Huerga and Popper (2), the zinc sulfate turbidity of Kunkel (3,4), the cephalin cholesterol flocculation of Hanger (5) and the thymol turbidity of Maclagan (6). Other tests like the Takata-Ara test (7), the colloidal gold (8) and red (9) tests, the cadmium sulfate (10) turbidity follow similar principles. The basic alteration which is common to all tests referred to is an increase of the serum gamma globulins, the largest molecules of the serum proteins.

Elevation of serum gamma globulin is in no way specific for liver diseases but occurs also in rheumatic

diseases, rheumatoid arthritis, lupus erythematosus, tuberculosis, Boeck's sarcoid and various chronic infections as well as plasma cell myeloma. Moreover, a slight elevation above normal was observed in a not insignificant percentage of apparently healthy blood donors (2). Nevertheless, the gamma globulin elevation if taken against the proper background may be of help in the follow-up of hepatic diseases. Of the tests mentioned the gamma globulin turbidity reflects only variations in the serum gamma globulin concentration and the results of this simple test correlate sufficiently well with those of electrophoretic partition to permit its use in the clinical laboratory (11). The upper limit of normals is 1.25 gr. per cent and in liver disease elevations are rather commonly encountered (12). In severe viral hepatitis (Table I) the elevation is rarely absent and in one-third of the cases the values exceed 2 gr. per cent. Even in the mild form as well as in the recovered stage the values were still slightly elevated. In the chronic form they were rather consistently and markedly elevated. The gamma globulin turbidity mirrors thus well the severity of viral hepatitis. The cases of cholangiolitic hepatitis revealed normal values. In toxic hepatitis an elevation was fairly common. The highest values were observed in cirrhosis especially so in the forms with jaundice. In these, elevation above 2 gr. occurred in almost all. In jaundice, produced by extrahepatic mechanical obstruction due to stones, tumors or scars the elevation though regularly found is usually slight. But the elevation is still sufficient to deprive this test value in the differential diagnosis between surgical and medical jaundice.

The gamma globulin is in contrast to many other serum proteins known to be formed by lymphatic (13, 14) and reticuloendothelial (15) elements, in the liver probably by Kupfer cells and mesenchymal elements in the portal triads (12). The elevation of the gamma globulins in liver disease is apparently due to a proliferation of the Kupfer cells and other mesenchymal

TABLE II. RESULTS OF CEPHALIN CHOLESTEROL FLOCCULATION AND THYMOL TURBIDITY TESTS IN HEPATO-BILIARY DISEASES

Diagnosis	No. of Cases	Cephalin flocculation		Thymol turbidity		
		Mean	% of 2 plus and above	Mean	% of above units	% of above units
Severe viral hepatitis	51	3.3	92.0	13.5	90.2	74.5
Mild viral hepatitis	27	1.8	59.2	6.5	66.7	22.2
Recovered viral hepatitis	33	1.3	45.5	5.0	69.8	21.2
Chronic viral hepatitis	14	3.3	93.0	13.7	78.6	78.6
Cholangiolitic hepatitis	5	0	0	6.4	60.0	40.0
Toxic hepatitis	44	1.7	57.8	6.8	40.9	27.3
Cirrhosis with jaundice	93	3.4	89.2	8.4	93.4	44.0
Cirrhosis without jaundice	67	1.6	53.9	6.3	47.8	29.9
Obstructive jaundice	55	1.0	32.8	4.6	26.3	14.0

elements. They are stimulated in viral and also in toxic hepatitis and especially so in cirrhosis with severe liver cell damage. In obstructive jaundice the mesenchymal cells are loaded with bile pigment to a degree which interferes with gamma globulin formation. Whether this increased gamma globulin formation in the mesenchymal cells is an expression of immune body formation is questionable. However, even if immune body formation should occur either due to a virus in viral hepatitis or to liver cell break-down products in the other hepatic conditions (16), quantitatively the amount of gamma globulins are much higher than they are usually found during antibody formation produced by very active immunization. Therefore, this excess globulin is probably a non-specific product of the stimulated hepatic mesenchyma, a so-called "reaction" globulin (17). This antibody formation may cause the excessive gamma globulin formation (12). It should be noted that in cirrhosis in which the serum gamma globulins are the highest the fibroblast stimulation is possibly due also to the liver cell breakdown products. This suggests that both mesenchymal reactions in the liver, namely the gamma globulin production and the fibroplasia, are related to each other (12). In principle, therefore, abnormal results in gamma globulin turbidity indicate a mesenchymal reaction which is not necessarily located in the liver.

The zinc sulfate turbidity is also supposed to indicate globulin elevation, however, its results fail to reveal as significant a correlation with electrophoretic determinations of gamma globulin as the gamma globulin turbidity (11). The results of the zinc sulfate turbidity (which normally does not exceed 12.5 units) if the readings are based upon the standard curve by Shank and Hoagland (18), are similar in most instances to that of the gamma globulin turbidity. Thus, conforming with observations of others (4, 19, 20) in severe viral hepatitis a regular elevation was noted and in one half of the the gamma globulin turbidity. Thus, conforming with observed (Table I); in the other hepatic diseases the ele-

vation followed much the same pattern as the gamma globulin turbidity though it was less marked in cirrhosis. However, in sharp contrast to the gamma globulin, the zinc sulfate turbidity values were much lower in extrahepatic biliary obstruction than in the hepatic diseases and in this respect (which represents the main problem in the differential diagnosis of jaundice) the zinc sulfate turbidity is far superior to the gamma globulin turbidity. The explanation for this finding is the fact that the zinc sulfate turbidity is influenced by several additional factors which play no role in the gamma globulin turbidity. One is that it is depressed by a high serum albumin concentration. More important is the fact that biliary substances in the serum depress the turbidity as one can note if whole bile is added to serum in concentrations found in the blood in obstructive jaundice (12). This material apparently regurgitates in obstructive jaundice into the blood and acts as a depression factor which gives this test its special diagnostic value.

The cephalin flocculation also depends on gamma globulin elevation. In this test, however, changes in serum albumin are of even greater importance in that reduction of the albumin level produces flocculation (21,22). Even in cases with normal ratio between albumin and gamma globulin the cephalin flocculation may be 4+. This observation indicates that qualitative changes of the albumin (as they occur in liver cell damage) may produce or exaggerate the flocculation. Serum albumin is formed by the liver cells; it is easily understandable that damage of these cells reduces or changes serum albumin. In this sense the cephalin flocculation indicates damage of the liver cells themselves in contrast to the above tests. This is in keeping with the observation that of all the tests studied, the cephalin flocculation revealed the best statistical correlation with histologically visible liver cell damage (23). The results in the studied series as well as studies reported by many authors (1) support this finding in that (Table 2) cirrhosis with jaundice and severe viral

TABLE III. PERCENTAGE OF COMBINED INCIDENCE OF ABNORMAL CEPHALIN FLOCCULATION (2 PLUS AND MORE) AND THYMOL TURBIDITY (MORE THAN 5 UNITS) IN HEPATOBILIARY DISEASES

Diagnosis	Percentage incidence of			
	Cephalin Flocculation: Thymol Turbidity	Abnormal : Abnormal	Abnormal Normal	Normal Abnormal Normal
Severe viral hepatitis		86.4	7.8	3.9 1.9
Mild viral hepatitis		48.2	7.4	18.5 25.9
Recovered viral hepatitis		34.5	6.9	6.9 51.7
Chronic viral hepatitis		76.9	15.3	0 7.7
Cholangiolitic hepatitis		0	0	60.0 40.0
Toxic hepatitis		42.2	17.7	4.4 35.6
Cirrhosis with jaundice		71.4	16.4	7.1 5.1
Cirrhosis without jaundice		38.8	13.4	14.9 32.8
Obstructive jaundice		8.8	22.8	12.3 56.0

hepatitis revealed the highest incidence of abnormal results (2+ and over). Mild and recovered viral hepatitis revealed lower and cholangiolitic hepatitis normal values. Obstructive jaundice, however, showed usually normal results; even in the presence of liver cell damage (biliary hepatitis) which may tend to reduce or change the serum albumin, the lack of the gamma globulin elevation as well as the biliary depression factor mentioned above keep the flocculation down. Exceptions are instances in which a secondary bacterial infection may elevate the flocculation tests.

The thymol turbidity depends to a similar degree as the cephalin flocculation upon the elevation of gamma globulin and upon reduction and alteration of serum albumin. In this test, however, in addition the serum lipoprotein and lipids tend to increase the turbidity (24). Aside from the lipid effect which has also been used for measuring lipid absorption (25), the results of the thymol turbidity follow that of the cephalin flocculation; it also indicates liver cell damage as the above-mentioned statistical studies have indicated (19). The results in this study as well as those of other investigators (1) were similar to those of the cephalin flocculation (Table 2) except that in cirrhosis with or without jaundice and also in toxic hepatitis the elevation above the normal 5 units (by use of the standard curve of the Shank and Hoagland) (18) was not as common as in viral hepatitis; also marked elevation (above 8 units) was relatively rare.

The combination of the results of cephalin flocculation and thymol turbidity (Table 3) increased the incidence of abnormal results in the medical type of jaundice whereas only rarely both tests were abnormal in obstructive jaundice and if so rather the cephalin flocculation was abnormal than the thymol turbidity. This

holds true for acute and chronic hepatitis and cirrhosis. In the cholangiolitic type of hepatitis, the cephalin flocculation was consistently negative. This lesion represents the greatest difficulty in the laboratory diagnosis of jaundice, because the absence of liver cell damage and the supposed involvement of the smallest intra-hepatic bile ducts (26) produces a picture characteristic of surgical jaundice in a medical condition.

Summarizing, then, the presented viewpoints, it appears that the mesenchymal reaction influences primarily gamma globulin and zinc sulfate turbidity and less so the other two flocculation tests. In the latter, liver cell damage makes itself significantly felt due to quantitative and qualitative albumin changes. The depressing factor of regurgitated biliary material is pronounced in the zinc sulfate turbidity but occurs also in the two other tests, whereas the lipid concentration influences measurably the zinc sulfate and the thymol turbidity tests (Table 4).

If we now try to develop a workable scheme of these four tests we come to the following flocculation profile (Table 5). In hepatitis cephalin flocculation and thymol turbidity are markedly, gamma globulin and zinc sulfate turbidity moderately abnormal. In toxic hepatitis the incidence of normal flocculation tests is a little higher, because of the less marked mesenchymal reaction (e. g. in 24.4 per cent of all studied cases cephalin flocculation, zinc sulfate and thymol turbidity were normal). In transition into cirrhosis a rise of the gamma globulin is observed. In the fully developed cirrhosis, gamma globulin is very high whereas the cephalin flocculation is, in the jaundiced cases, usually elevated, however, the thymol turbidity irregularly so.

TABLE V. FLOCCULATION PROFILE

TABLE IV. FACTORS DETERMINING OUTCOME OF FLOCCULATION REACTIONS

	Gamma Globulin	ZnSO ₄ Turbidity	Cephalin Flocculation	Thymol Turbidity
Mesenchymal reaction	+++	++	+	+
Liver cell damage (altered or reduced albumin)	0	+	+++	++
Depression due to biliary obstruction	0	++	++	+
Lipid elevation	0	++	0	+++

	Gamma Globulin	ZnSO ₄ Turbidity	Cephalin Flocculation	Thymol Turbidity
Acute hepatitis	++	++	+++	+++
Transition into cirrhosis	+++	++	0	±
Cirrhosis with jaundice	+++	+++	++	0-++
Cirrhosis without jaundice	+++	++	+	0-+
Obstructive jaundice	±	0	0	0-±

TABLE VI. COMBINED USE OF CEPHALIN FLOCCULATION AND THYMOL TURBIDITY TESTS IN 449 CASES WITH JAUNDICE FOR THE DIFFERENTIATION BETWEEN MEDICAL AND SURGICAL CONDITIONS

449 cases cephalin flocculation				
	0 and + 151 cases		++ to ++++ 298 cases	
zinc sulfate turbidity in units	below 12.5 73 cases	above 12.5 78 cases	below 12.5 42 cases	above 12.5 256 cases
Assumed Diagnosis	Surgical		Medical	
Percent error	16.4	90	35.7	3.9
Diseases causing error	3 cirrhosis 2 cholangiolitic hepatitis 2 toxic hepatitis 5 viral hepatitis	5 biliary hepatitis 2 infected biliary hepatitis	5 biliary hepatitis 10 infected biliary hepatitis	5 biliary hepatitis 4 infected biliary hepatitis

If the cases of infected biliary hepatitis (clinically recognized by signs of septicemia are omitted, there were 15 wrong diagnoses in 376 medical cases (error of 4.0%) or 27 wrong diagnoses in a total of 449 cases (error of 6.0%).

In contrast, in obstructive jaundice zinc sulfate turbidity, cephalin flocculation and thymol turbidity are low whereas gamma globulin turbidity is on the border line. (In 25.6 per cent of the studied cases, of the four tests, only the gamma globulin turbidity was elevated). This presents a workable scheme for the differential diagnosis between medical and surgical jaundice provided that the following exceptions are taken into account. In the cholangiolitic and toxic hepatitis false negative tests are corrected by the clinical history and false positive tests in obstructive jaundice, as caused by secondary bacterial infection, are clinically recognized by evidence of septicemia such as fever, chills and leukocytosis.

If one attempts to simplify this profile by the use of only two tests, it appears best to omit the gamma globulin and the thymol turbidity, the former due to its elevation in obstructive jaundice and the latter omission is explained by the following findings in this series: the thymol turbidity was normal while the cephalin flocculation and zinc sulfate turbidity were elevated in 14 per cent of the cases of cirrhosis with jaundice, in 9.2 per cent of cirrhosis without jaundice and in 12.2 per cent of toxic hepatitis (the thymol turbidity is especially useful in the differentiation of acute hepatitis and cirrhosis). In acute hepatitis the thymol turbidity is much higher relative to the zinc sulfate turbidity while in cirrhosis the reverse is true (20). In table 5 (which reviews the results in 499 cases of jaundice) enlarging upon previously reported observations (20), the diagnostic results are visualized which are obtained by assuming that cases with positive cephalin flocculation and those with negative cephalin flocculation but elevated zinc sulfate turbidity are medical, whereas those in which both are normal are surgical. In such a scheme errors were encountered in each of the four groups of which the most common was the assumption of a medical condition in a patient with biliary hepatitis (due to extrahepatic biliary obstruction) with associated bacterial infection. Since the latter condition

can easily be recognized by the clinical manifestations of septicemia a relatively high percentage of expected results can be obtained in this combination of two tests. After exclusion of the infected biliary hepatitis in the studied series the error amounted to 6.0 per cent.

SUMMARY

Diagnostic results of flocculation tests in a large series of cases of jaundice are presented and the physical chemical basis of four tests used in the differential diagnosis of jaundice (cephalin cholesterol flocculation, thymol turbidity, zinc sulfate turbidity and gamma globulin turbidity) as well as the pathologic significance of the abnormal results is discussed. The following important factors are listed: liver cell damage, mesenchymal reaction, a biliary depression factor resulting from regurgitation and the serum lipid level. A consideration of these points offers a basis for the coordinated use of these technically simple tests in a flocculation profile. For the differential diagnosis of jaundice, the combination of cephalin flocculation and zinc sulfate turbidity appeared theoretically the most promising and practically the most effective.

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RESEARCH VIEWS ON GASTRO-DUODENAL ULCERATION

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IN THE COURSE OF medical history it is sometimes necessary to set aside current theories on a given subject, particularly when ideas of the pathogenesis cease to shed further light on the etiology and treatment of the disease in question. This appears to be true in the case of ulceration in the digestive tract.

For 80 years it has been held that gastro-intestinal ulcers were chemically-caused lesions of the mucous membrane which hollowed themselves out from the surface to the depths of the tissue. On the contrary, we have proved that gastrointestinal ulcers originate in the submucous portion of the wall and proceed from the depths to the surface.

TWO KINDS OF PROOF

1.—It was believed that ulcers of the gastric mucosa were caused by an excess of HCl in some unelucidated manner, autodigestion being fostered by an absence of protective mucus or by the chemical modification of the gastric mucus. But in France and Belgium it is a known fact that 25 per cent of ulcer patients do not show excessive acid secretion, many of them even showing subacidity, and in any case the prolonged absorption of large quantities of HCl does not produce gastro-duodenal ulcers (Bonorino-Udaondo). Neither sub-

total gastrectomy nor bilateral vagus resection—procedures which reduce free HCl—prevent the return of ulcers. Orr and Johnson showed that in 25 per cent of 215 vagotomized patients ulcer symptoms persisted or actual ulcers recurred following operation.

2.—Decisive proofs arise from studies in human and experimental pathological anatomy. The gastroduodenal ulcer is a crater, the bottom of which lies on the muscularis mucosae and may even penetrate still further to cause perforation. It is surrounded by vascular and hemorrhagic lesions (endothelitis, sanguine suffusions and hemorrhages) and as the blood vessels form a close network in the submucous tissue, one realizes that the vascular lesions of the ulcer begin here, and that the death of the superjacent mucosa results from shutting off of its blood supply by the thromboangiitis involved. The ulcer of Cruveilhier is thus the result of a mucous eschar and a form of necrosis of hemorrhagic type. It differs from the superficial ulcers which originate in the mucous membrane and are not surrounded by vascular lesions. Such is the ulceration of biliary origin observed in the rat subjected to stress.

We felt it safe to predict that if the tissues of an ulcer-bearing stomach were examined, we would find such hemorrhagic and vascular lesions but without damage to the mucous membrane. This prediction has now been vindicated. In a study of twenty stomachs resected for peptic ulcer we found gastritis in most of them, and in half of them definite foci of vascular lesions, sometimes congestion with erythrodiapedesis, considerable blood infiltration separating the muscular fibers, sometimes arteriolitis with lesions of the media

(Prof. Bernard's recent voluminous writings in French and Belgian medical journals on the subject of gastrointestinal ulceration, including idiopathic ulcerative colitis, from the standpoint of the role of the neurovegetative system in their production has attracted wide interest. In the present article Prof. Bernard summarizes his work for our readers. EDITOR)

JUNE, 1951

of the larger vessels, and hemorrhagic infiltration around the follicles.

We emphasize that these foci of vascular lesions were covered with intact and healthy mucous membrane which showed at most a slight depression and color change perceptible by gastroscopy. This focal vasculitis may be observed in all parts of the ulcer-bearing stomach even at a distance from the ulcer itself, but they are more commonly found on the opposite wall in kissing ulcers, or along the curvatures at the same level as the ulcer. Some of these foci of vasculitis terminate in true ulcers, others are cured without leaving a trace, while still others leave merely a depression of the mucous membrane. I have named such foci, *pre-ulcers*. They explain the production of multiple ulcers and the recurrence of ulcers through a reactivation of the focal vasculitis. Gastric hypersecretion and alterations in the mucous itself are of secondary importance in ulcer etiology as compared with the form of gastritis just described. In the bulb, when sections are made through the whole organ, pre-ulcers are constantly found facing the ulcers.

METAMERIZATION OF LESIONS

The three lesions constituting the ulcerous disease, —gastritis, ulcer and pre-ulcer,—have a metamerization, being placed on one and the same horizontal segment of the stomach, and the same horizontal arrangement is found in the bulb, the prepyloric cavity and fundus. This unmistakable metamerization of the lesions could not take place except for the participation of the neurovegetative system. When one remembers the intimate connections between the nervous system and the capillary vessels it becomes easier to understand that the metamerization of these lesions is the result of focal neuro-vascularitis. Only on such a basis can we explain the formation of kissing ulcers, the distribution of hemorrhagic foci in the experiments of Luigi Durante and of Reilly, as well as the horizontal irradiation of the pains of peptic ulcer.

The participation of the sympathetic system appears

also in other diseases, particularly rheumatoid purpura. I noted the part played by focal neurovascularitis in a 16-year-old patient, who in the course of rheumatoid purpura developed an ileal perforation and, seven years later a duodenal perforation. Histological examination showed the same vascular lesions not only around the ulcers but also at a distance from them. They were exclusively situated at a submucous level and could only be explained by the participation by a nervous system particularly predisposed in this patient.

The pathogenesis of gastro-duodenal ulcer involves focal neurovascularitis ending in the ulcer scar of the mucous membrane. This same process is to be observed at other levels of the gastro-intestinal tract. After attacks of ileitis and of ulcerative colitis foci of vascular lesions can be found under the mucous membrane at some distance from the ulcers.

Vasculitis is not an infectious process but a vascular alteration in the wall of the organ, accompanied or not by hemorrhage. While the neuro-circulatory mechanism of ulcer disease thus appears clear, it remains for us to study the possible causes which bring such a mechanism about.

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ABSTRACTS ON NUTRITION

SMITH, E. L.: *The vitamin B₁₂ group of factors*. *Brit. Med. J.*, Jan. 27, 1951.

It has been possible to obtain in crystalline form two further members of the vitamin B₁₂ group of factors, viz. vitamin B_{12c} and B_{12d}. Both these factors, on clinical assay, appear to act exactly as vitamin B₁₂, exerting the same control on hematological, lingual and neurological manifestations of the disease. (See in the same issue of B. M. J. the articles by Ungley on vitamin B_{12c} and by Chalmers on vitamins B_{12c} and B_{12d}). It has been shown that the vitamin B₁₂ molecule contains a cyanide group coordinated with the cobalt atom. A large portion of the molecule comprises 5:6-dimethyl-benzaminazole in glycoside linkage with a molecule of ribose phosphorylated at C₂ or C₃. The cobalt-containing atom is attached to this phosphorus atom, and it represents about two-thirds of the molecule. In addition, ammonia and 2 molecules of D-1-amino-2-propanol are attached somewhere. There is little doubt that the intrinsic factor of Castle is simply vit. B₁₂ itself.

Vitamin B₁₂ diminishes the excessive urinary excretion of phenols which occurs in pernicious anemia. This may be connected with the suggested toxic factor of pernicious anemia which ceases on administration of vitamin B₁₂. The only present clue to the hematopoietic action of the vitamin is its suggested function in the building of nucleic acids.

CONWAY, N. S. AND CONWAY, H.: *Vitamin B₁₂ and folic acid in megaloblastic anemia after total gastrectomy*. *Brit. Med. J.*, Jan. 27, 1951.

The authors describe a case of megaloblastic anemia following total gastrectomy performed for the effects of corrosive poisoning. Striking clinical improvement followed vitamin B₁₂ therapy, but the hematologic response was suboptimal, compared with that expected in Addisonian pernicious anemia. The addition of folic acid brought about complete hematological remission. Though morphologically similar to pernicious anemia, this anemia was not identical with it.

MENEGHELLO, J., NIEMEYER, H. AND ESPINOSA, J.: *Liver steatosis in undernourished Chilean children. I. Evolution*

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as followed by serial puncture biopsies. *Am. J. Dis. Child.*, Dec. 1950, 889-897.

The histologic changes of the liver in plurideficiency dystrophy were studied in 63 children and the existence of an intense fatty infiltration was proved. This disappears slowly in about 2 months of hospital care.

NIEMEYER, H. AND MENEGHELLO, J.: *Liver steatosis in undernourished Chilean children. II. Study on some liver function tests.* *Am. J. Dis. Child.*, Dec. 1950, 898-904.

Liver biopsy pictures were compared with simultaneously performed flocculation tests in children suffering from fatty infiltration of the liver associated with plurideficiency dystrophy, but there was a negative correlation between the degree of fatty infiltration and the amount of flocculation. Carbohydrate tests of function showed a better, though imperfect, correlation with the biopsy specimens.

HICKS, M. H. AND LEAVELL, R. S.: *Pernicious anemia in the American negro.* *Ann. Int. Med.* 33, 6, Dec. 1950, 1438-43.

The authors believe that the pure-blood American negro is not immune to pernicious anemia and that the true incidence of the disease in negroes probably is equal to that in whites. The symptomatology of the disease is the same in both races. The response to liver therapy in negroes was found to be inferior to that which occurred in white patients. This inferior response seems to depend upon some racial factor at present unrecognized.

LONIE, T. C.: *Excess vitamin A as a cause of food poisoning.* *New Zealand Med. J.*, Dec. 1950, XLIX, 274, 680-685.

A family outbreak of food poisoning due to consumption of shark liver is recorded. The symptoms and signs resemble those recorded as due to consumption of polar bear liver, and considered to be due to excess vitamin A. Shark liver such as that consumed, has a high vitamin A content and the author presumes that the cases recorded were due to hypervitaminosis A. Headache, nausea, vomiting, dizziness, came on soon after eating the shark liver and were followed, in 36 hours, by extensive desquamation, commencing around the mouth but extending over the whole body. The liver eaten probably contained 165,000 I. U. per gram of weight.

YANAGISAWA, F. AND MIZOKOSHI, M.: *The colorimetric estimation of free and combined cholesterol in serum.* *Japanese Med. J.*, 3, 2, Apr. 1950, 137-140.

By modifying Zuckerman's method of cholesterol determination, the authors found a rapid method for free and combined cholesterol. The total cholesterol is first determined by Zuckerman's method. Combined and free cholesterol are determined on the chloroform extract with the aid of digitonin. Free cholesterol is in the digitonin precipitates and the combined cholesterol remains in solution. The results by their method are compared with those obtained by the methods of Sperry and Pijoan, showing a positive variation from 2 to 5 percent.

TAKAOKA, Y., OZAKA, K. AND YAKAWA, S.: *Hypertrophy of parotid glands in diabetes mellitus and internal secretion of salivary glands.* *Japanese M. J.*, 3, 3, June 1950, 199-203.

The authors claim to have noted that the parotid glands are enlarged in 80 per cent of diabetics, at times when the disease is under control. They also claim to have extracted a blood-sugar lowering substance from the salivary glands of 5 alloxan diabetic dogs. They believe that the salivary glands play a compensatory role to the pancreas in the regulation of carbohydrate metabolism.

SMITH, C. A.: *Nutrition of premature infants.* *Nutrition Reviews*, 8, 12, Dec. 1950.

A premature infant must be fed carefully to prevent aspiration of improperly administered food, but the nature of his diet appears to be of less importance. Nutrition is of less significance in determining whether the premature infant will live to grow than in determining the satisfactoriness of his growth if he lives. There is a unique requirement for ascorbic acid to allow complete metabolism of the aromatic amino acids in premature existence. Cow's milk probably is preferable to human milk for mineralization of the skeleton. The pediatricians have not yet decided which kind of milk is the better for premature infants. Supplementation is necessary in either case. The anemia which develops early does not respond well to any treatment. There is a large requirement of vitamin D to prevent rickets. The most serious of the unsolved problems of prematurity is retrolental fibroplasia, which develops in the eyes some weeks after birth and often progresses to more or less complete blindness. It occurs in from 5 to 20 per cent of infants weighing less than 4 pounds.

PALMER, L. J., TRUESDELL, D. E., FLAHERTY, N. F. AND CRAWFORD, J. H.: *NPH insulin: clinical results.* *Bull. Mason Clin.*, 4, 4, Dec. 1950.

The authors used NPH insulin (crystalline protamine zinc insulin of Hagedorn) on 28 patients over a two-year period and found that the use of NPH insulin gave improved control of the blood sugar level and a lowered incidence of hypoglycemic reactions. In all cases requiring the use of mixtures, NPH insulin is more simply and accurately administered.

BRAM, I.: *Psychic factors in obesity.* *Arch. Pediat.*, 67, 12, Dec. 1950.

Alimentary obesity is a psychosomatic condition in which the psychic is responsible for the somatic plight. Conviction and persuasion are the two elements of effective argumentation to be employed in psychotherapy. The doctor must convince the patient of the facts involved in the quest for normal weight, and persuade him to act promptly on this conviction by sincere cooperation. Re-education of life-long concepts of eating and nutrition is the therapeutic need.

PETERSON, J. E. AND HIRST, A. E.: *Studies on the relation of diet, cholesterol and atheroma in chickens.* *Circulation*, III, 1, Jan. 1951, 116-119.

100 cockerels were fed various diets, supplemented with lard, vegetable oil and vegetable oil with added cholesterol. The degree of atherosclerosis in these birds was compared at serial autopsies, and only the cholesterol-fed group showed significant difference. In this latter group severe atherosclerosis developed rapidly and there was a considerable increase in the lipid content of the liver. Observations in a small group of chickens suggest that if feeding of excessive amounts of cholesterol is stopped in time, there may be some reversal of the atheromatous lesions. Later the regression of such lesions may be much less complete.

OSSEMAN, K. E. AND DOLGER, H.: *Obesity in diabetes: a study of therapy with anorectic drugs.* *Ann. Int. Med.*, 34, 1, Jan. 1951.

36 of 55 obese diabetic patients showed significant loss of weight on low caloric diets aided by benzedrine, (Gr. X, 3 times a day) and by dexedrine, (Gr. X, 3 times a day), the latter isomer being used in hypertensive cases. Usually 1,600 cal. per day were permitted. Weight losses varied from 11 lbs. to 77 lbs. Of 31 patients using insulin, 15 were able to discontinue it and 11 obtained dosage reduction after weight loss. No immediate adverse effects of the drugs were noted.

EDITORIAL

SCIENCE AND THE PHYSICIAN

Even for the ultra-specialist, restricting his attention to the most limited fields, it has long since become practically impossible to keep informed on much of the current scientific advances. Thus the gastroenterological roentgenologist can scarcely stay abreast of what is published every week on this subject alone. The internist and general practitioner particularly are likely nowadays to develop a severe inferiority complex in their attempts to refashion their ideas and methods in conformity to the changing horizons in cardiology, in psychiatry and other departments too numerous to designate. A partial cure for this unpleasant sense of inferiority might be found, if the physician were physically able to study all night, following every hard day's work. Even then, the solution would be but a partial one. The universal mind in medicine is so anachronistic today that it appears to be forever doomed to extinction.

However, we may take heart, in spite of the restrictions imposed upon us by time and by the unprecedented evolutions taking place in medicine as a whole. It is important, while we are confronted on every hand by complicated and specific ad-

vances in diagnosis and therapy, to remember that there are a number of basic truths which remain steadfast and uninfluenced by the progress of science. Thus, if a physician can tell whether a given patient is ill or not, he is in possession of a faculty indispensable in practice and yet one which is not too common. When in doubt about some important aspect of a case, if he has the restraint to do nothing, he is a safe practitioner. If, on the whole, he is able, as a rule, to arrive at a diagnosis in a reasonable length of time, he is useful in his profession. Finally, if the stores of his knowledge, the quickness of his wit, the facility of his memory and his industry are matched by a sympathetic and intuitive nature, he is not only a credit to his profession but also an indispensable member of his community. The impossible can seldom be accomplished, but the possible seldom is completely explored.

ERRATUM

In the article "A Study of Laboratory Methods for Diagnosing Endamoeba Histolytica and Their Application to 5,048 Persons From the Chicago Area" which appeared in the April issue, the first line of the Summary on page 130 should read "The paper presents a compilation of extensive studies."

GÖSTA FORSELL
In Memoriam

Gösta Forsell was born 2nd of March 1876 and died 17th of November 1950. Professor Berven characterizes him as a pioneer and organizer, scientist and teacher, healer and lover of mankind and one of the most noble sons of Sweden. He was head of the Roentgen Institute of the Serafimerlasarettet 1906-1941, Director of the Radium Home 1910-1926. Professor of medical radiology of the Karolinska Institute from 1917-1936, when the professorship was divided in two. He was then professor of roentgen diagnosis from 1936 until 1941, in which year he retired.

Forsell has developed the specialty of roentgenology to an independent branch of medicine in Sweden and after this pattern in many other countries. He saw the importance in the centralization of radiology, diagnostic as well as therapeutic, in well equipped independent departments with their own organization, doctors and nurses.

Gösta Forsell succeeded in bringing the radiology of Scandinavia together in the Northern Association of Medical Radiology in 1919. Forsell then founded Acta Radiologica and has been editor and chief until the time of his death.

Forsell's scientific works comprise more than 200 papers covering the most diverse fields in radiology and other sciences. Those who wish to know more about Gösta Forsell's life and his work,—it is quite fascinating to read about it,—can find a description of this in Acta Radiologica for December 1950, written by Professor Berven and Professor Akerlund. Of special interest for the readers of this journal must be the fact that it was the alimentary tract and especially the

stomach and its movements which was Forsell's great interest in the fields of roentgen anatomy and roentgen physiology, and it was on this subject that he wrote his great thesis for his degree in 1913.

Forsell showed that the mucous membrane of the stomach by an inherent reflex mechanism in its own musculature could alter the size of the stomach's lumen independently of the state of contraction of the muscles in its wall. He showed that the mucous membrane pattern in one and the same place could change in appearance from one moment to another in spite of the absence of any alteration in the size of the lumen. This is what Forsell called the autoplasticity of the mucous membrane. He showed that the autoplasticity of the mucous membrane depends upon the contraction of its own musculature, the muscularis mucosae. He has also shown that this autoplasticity is of the greatest importance in the digestion process. For the roentgenology it is of basic importance to know these great normal variations in the picture of the mucous membrane caused by this autoplasticity of the mucous membrane. One can say it is necessary for every radiologist to know these things in detail if he wishes to be able to give a correct description of a roentgenogram from a normal or pathologically changed mucous membrane.

In his article about Gösta Forsell professor Ake Akerlund says: "His name will forever stand as one of the very greatest and most brilliant in the international clinical radiology."

O. W. Husebye, M. D.
Oslo, Norway.

BOOK REVIEWS

A CLASSIFIED BIBLIOGRAPHY OF GERONTOLOGY AND GERIATRICS. Nathan W. Shock, 599 pages, Stanford University Press, Stanford, California, 1950, \$15.00.

An extremely exhaustive listing of just about all that has been written on the biology of aging, the organic systems in the aged, the art of geriatrics, and the psychology and the social and economic aspects of senescence. Over 18,000 journal and book references are gathered together. One is overwhelmed by the tremendous scope and thoroughness of the volume,—one which most physicians should possess in view of the current increase in life expectancy.

CHRONIC ULCERATIVE COLITIS. J. Arnold Barges, M. D., 62 pages. Charles C. Thomas, Springfield, Illinois, 1951, \$2.00.

It is probable that Barges has seen more cases of ulcerative colitis than anyone who ever practiced medicine. The present monograph is an excellent description of the disease in all its manifold forms, and breathes the tempered optimism of its author,—a mood that has proved of value in actual treatment of patients. Barges regards the disease as a severe intestinal infection,—a somatic affliction, which does not permit a purely psychological evaluation from the etiological

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standpoint. He emphasizes two points of value,—that the disease is much less serious when it begins after 60 years of age, and that, in most adults, recurring attacks tend to become milder. In many it becomes arrested under skilful management. The medical and surgical treatment are given in detail. The book should prove very valuable to all physicians.

ANNOTATED BIBLIOGRAPHY OF VITAMIN E, 1940-1950. Philip L. Harris and Wilma Kujawski. 184 pages. The National Vitamin Foundation, Inc., 150 Broadway, New York 7, N. Y., 1951, \$3.00.

Vitamin E was discovered in 1922. During the decade 1940-1950, there were more than 1500 scientific publications and patents concerned with this vitamin. Vitaminologists who restrict their attention to vitamin E are unable to keep abreast of publications,—consequently physicians find it an utter impossibility. Some 1562 references are printed and, in most instances, a summary is included of the contribution quoted. Such a compilation represents a tremendous amount of research and

the results will prove indispensable to those interested in the vitamin. The scientific aspects are dealt with first and then there are over 400 references dealing with the therapeutic value of vitamin E in medicine. That the subject still represents, to some extent, a medical field of romance is obvious from the contrasting results obtained by various physicians in not a few pathological conditions. The influences of vitamin E in cardiovascular disease are no more disputations than in other fields. Time alone can settle the true medical value of vitamin E.

THE NUTRITIONAL CONTRIBUTION OF BREAKFAST CEREALS (A TEACHER'S SOURCE BOOK). Clara Mae Taylor. Cereal Institute, Inc., Chicago 3, Ill., 1951. Gratis.

A 20 page brochure on the title subject is of considerable interest because of its wide-angle approach. The importance of an adequate breakfast receives repeated emphasis. Recommended dietary allowances and meal patterns are presented in a constructive manner.

GENERAL ABSTRACTS

SEEDORF, E. E., POWELL, W. N., GREENLEE, R. G. and HARTMAN, J. T. *Prindox and pseudoalbuminuria*. Radiology 55, 5, 740. November, 1950.

A false positive reaction for albumin will occur in the analysis of the urine of a significant number of patients receiving the standard dosage of 6 tabl. of prindox. The fact that it is the actual presence of prindox in the urine which causes this reaction is proved by laboratory tests. The false albuminuria occurs with the greatest frequency in the lighter weight group and, therefore, in women and younger individuals. Other factors, such as prevailing barometric and temperature readings and the specific gravity of the urine examined, play no apparent role. Detectable amounts of prindox are present in the urine of certain patients not only on the morning after the ingestion of prindox, but the following day and occasionally even on the third day. "Albuminuria" occurring after administration of six tablets of prindox does not indicate renal irritation due to the drug.

Franz J. Lust

LEVI, L. M. and ENGLE, R. B. *Radiation therapy of acute pancreatitis; a report of 28 cases*. Radiology 54, 4, 576. April, 1950.

A series of 28 cases of acute pancreatitis treated by irradiation is reported. Of the series, two patients died: one as a direct result of the disease and its complications; the other six months later, of delirium tremens. Both patients had normal urine and serum diastase levels shortly before death. At autopsy, both had evidence of residual pancreatitis with necrosis. The clinical impression gained is that some patients may obtain relief from vomiting, nausea, distention, or pain.

Franz J. Lust

INGRAM, M. D. *Gastric ulcer in childhood*. Am. Journal Roent. Rad. Th. 64, 5, 765. Nov., 1950.

Gastric ulcer in children is a rare occurrence. Of the 33 cases reported in the literature, five were found at autopsy, thirteen by surgery, and fourteen by roentgen study. Nine of the latter group were confirmed by surgery. It is interesting to note that the first four cases reported in the literature were found at autopsy, the next thirteen cases were found at surgery. Of the remaining cases reported since 1932, comprising 15 cases, all but three were initially diagnosed from the roentgenological examination. Especially in the last years, ulcers were discovered by roentgenological examination.—In the reported case of an eleven year old child, the roentgenological examination revealed a crater of 2 cm. size on the lesser curvature of the stomach. Clinically there were sharp epigastric pains with vomiting of a coffee-ground material. There were no tarry stools. Complete recovery was seen after a Sippy regimen.

Franz J. Lust

FRIEDMAN, J. and RIGLER, L. G. *A method of double-contrast roentgen examination of the small intestine*. Radiology 54, 3, 365. March, 1950.

The technic of double-contrast visualization of the small intestines with use of a three-lumen Miller-Abbott tube is described, and the roentgen anatomy as demonstrated by this procedure is illustrated. The indications for this examination are: undetermined defects in the small intestine, suspicious areas, disordered motor function in which organic pathology is suspected. In cases of possible bleeding from the small intestine, constant aspiration is suggested with testing of with guaiac solution. If the test proves positive, the bowel is then examined at the site of bleeding. In cases of obstruction, the diagnostic use of the tube is also an adjunct in therapy, as a decompressive agent. Interesting are a case of adhesions and one of disordered motor function in pulmonary tuberculosis.

Franz J. Lust

SMELLIE, J. M., *Chloromycetin in infantile gastro-enteritis*. (Proc. Roy. Soc. Med., XLIII, 10, Oct. 1950).

Of 27 cases of gastro-enteritis in infants, mostly under 6 months of age, treated with chloromycetin, only one died, and all the others improved. In a few instances the favorable responses were dramatic. The dose used was 75 mg. per pound of body weight per day, at 3 or 4 hourly intervals. The drug produced some increase of sore buttocks, stomatitis in a few cases, and cutaneous eruption in 2 cases. The results obtained with chloromycetin were more promising than have been achieved with other chemotherapeutic or antibiotic substances.

SLATER, M.: *Roentgenological diagnosis of sponge in the abdomen*. (Am. J. Roentg. & Rad. Ther., 64, 5, Nov. 1950).

A case is described in which a preoperative diagnosis of sponge in the abdomen was made and verified. The diagnosis was based on the persistence of a small, localized collection of small bubbles of air trapped in the mesh of the sponge. The collection of air is in a circumscribed area, the bubbles of gas are smaller and more uniform in size than intestinal gas, the gas bubbles are not surrounded by a limiting membrane and there was no change in the appearance when the patient's position was shifted and on separate days. If the diagnosis is considered, it is not likely to be mistaken for anything else.

ELROD, R. P., SANDERS, A. C. and HULLINGHORST, R. L.: *The isolation of three "Shigella paradysenteriae" serotypes from one patient*. (U. S. Armed Forces M. J., 1, 11, Nov. 1950, 1299-1300).

On previous occasions the authors have isolated two serotypes but are not aware of any previously reported case in which 3 types of organisms have been isolated from one patient, Types IV (Boyd 103) I, III, (VZ) and VI (Boyd 88). Large outbreaks of bacillary dysentery are often caused by more than one type. Since multiple infections confuse epidemiologic studies, the value of selecting several colonies is evident.

REDFIELD, E. S.: Isolated fat replacement of body and tail of pancreas. (U. S. Armed Forces M. J., 1, 11, Nov. 1950, 1313-1321).

A case is reported of almost complete fat replacement of the body and tail of the pancreas with normal pancreatic head and neck in a 75 year old diabetic negro. The most likely cause was acquired obstruction of the distal part of the main pancreatic duct. The diabetes probably was caused by the fat replacement. An island cell adenoma was present and may represent a compensatory phenomenon for the great loss of islet tissue.

INGRAM, M. D., JR.: Gastric ulcer in childhood. (Am. J. Roentg. and Rad. Ther., 64, 5, Nov. 1950).

Gastric ulcer in children is a distinct rarity. Such a case in an 11 year old boy is reported in which the diagnosis was made by x-ray. Of the 33 cases reported in the literature, 5 were found at autopsy, 13 by surgery and 14 by roentgen study. Of the 15 cases found since 1932, all but three were initially diagnosed from x-ray examination. All children with G. I. symptoms, especially hemorrhage, should have a thorough x-ray study of the gastrointestinal tract.

THOMPSON, A. W., and MULENBURG, R. A.: Scleroderma with apparent gastric involvement. Bull. U. S. Army Med. Dept. IX, 11, 929-933.

A 30 year old woman developed vasomotor changes in the extremities with a gradual collagenous thickening of the skin of the arms, legs, face and chest which justified a diagnosis of progressive generalized scleroderma. She had some symptoms referable to the upper gastro-intestinal tract and, although x-ray examination yielded negative results, gastroscopy revealed an abnormal condition of the gastric lining. The mucosa was pale and of a necrotic gray orange color. Surrounding the region of the cardia there was a band of pathological change extending 4 cms. below the esophagogastric junction, and similar changes could be seen in the lowermost portion of the esophagus. These regions appeared thickened, smooth, and shiny with an absence of rugae. Except for tiny superficial red vessels at the esophagogastric junction, there were no visible blood channels. These changes obviously should be accepted as part of the scleroderma syndrome.

C. L. OAKLEY: The toxins of *Cl. welchii* Type F. (Brit. Med. J., Feb. 12, 1949, 269-270).

The author examined 8 cultures obtained from cases of enteritis necroticans by Professor Zeissler. Briefly it was found that the chief toxin produced was beta-toxin, and the lethal qualities of this toxin were completely neutralized by beta-antitoxin. Therefore the causal agent of enteritis necroticans produces chiefly beta-toxin, although some alpha and some gamma-toxin was present.

HAIN, E.: Origin of *Cl. welchii* Type F infection. (Brit. Med. J., Feb. 12, 1949, 271).

The author reports a case of a man of 71 who, after eating home-canned, home-bred rabbit, died within 2 or 3 days of enteritis necroticans and from the pathological specimens and stools, *Cl. welchii* Type F was isolated. Two others who ate the same meat became ill but recovered. Although the tins containing the rabbit meat were closed and boiled for two hours in a water bath, this, as we know, would not kill the spores of Type F *welchii*. It is clear that the usual method of sterilizing meat by boiling for two hours will not suffice if it is contaminated with this organism.

LINN, H. W.: Occult blood in feces: the benzedrine test. (Med. J. Australia, Jan. 1, 1949, 15-16).

A series of experiments was done with the benzedrine occult blood test. The method used gave positive results with less than 0.01 milliliters of blood. A meat-free diet for 3 days is all the preparation required for the test. Iron compounds and meat extracts did not influence the outcome of the test.

HALBERT, S. P. and GRAVATT, M.: Prevalence of antibiotic-producing coliform organisms. (Public Health Reports, Mar. 11, 1949, Vol. 64, No. 10, 313-318).

Both foreign and American observers have studied large numbers of coliform organisms capable of producing antibi-

otic substances *in vitro*. Little information is available, however, as to whether such antibiotics are produced *in vivo* in the intestinal tract. Because of the possible implication of such microorganisms in the recovery from and resistance to *Shigella* infections, a study was undertaken to shed light on this question. A survey was made of the antibiotic producing capacities of fecal lactose-fermenting bacteria from an adult population in North Carolina. Of the 2,105 coliform strains examined, 24.8 per cent were active in this respect. Of the 108 individuals included in the study, 62 per cent carried such active strains. Tests were made with aqueous stool extracts from these subjects which failed to reveal evidence for antibiotic production *in vivo*. Many of these stools contained large numbers of coliform strains shown to possess the ability to produce antibiotics *in vitro*. The high prevalence of such strains in three widely operated sections of the U. S. A., together with reports of such strains from Belgium and England, suggest that they are universally distributed.

GROTTIS, R. F.: Fetal peritonitis. (Arch. Pediat., Jan. 1949, Vol. 66, No. 1, 1-8).

The author describes four cases of fetal peritonitis, all of which resulted in death. They were associated with intestinal malformations and/or cystic fibrosis of the pancreas. *E. coli*, pneumococci, and staphylococci were isolated in these cases. Early abdominal distention and vomiting were the chief signs, and calcified abdominal meconium plaques are often seen on the x-ray film. By earlier diagnosis and the use of modern anti-infective agents, it is hoped that a more successful therapy may be developed. Fetal peritonitis may cause death in utero, or the patient may die shortly after birth, the actual perforation, if present, taking place during labor. Some cases undoubtedly are aseptic peritonitis and some are due to pneumococcus, as revealed by paracentesis.

MACKERRAS, I. M. and MACKERRAS, M. J.: The bacteriological diagnosis of *Salmonella* infections. (Med. J. Australia, Jan. 1, 1949, Vol. 36, No. 1, 1-3).

The procedure used by the authors to isolate *Salmonella* from feces was as follows: (1) Plate the material directly on 'Difco' SS agar and inoculate tetrathionate broth, (2) Pick off colonies onto Mannite-Kligler medium (alternately inoculate ordinary Kligler medium and test any suspicious growth for urease production), (3) Test cultures giving a 'Salmonella reaction' for fermentation of lactose, glucose, mannite, sucrose and urea (if not used previously), for indole production, for motility, for reaction to Gram stain, and with polyvalent *Salmonella* agglutinating serum. These procedures economized time and materials and gave a reliability of about 60 per cent in acute stages and 80 per cent in later stages of *Salmonella* gastroenteritis in infants. In their experience, diagnostic cultures should be continued to not less than the sixth, and clearance cultures during convalescence to not less than the third, before a *Salmonella* infection is excluded. Positive results may be reported in 3 days from the direct plate in more than half the cases, in 4 days from the tetrathionate broth in the remainder. An indication may be given 24 hours earlier by direct agglutination from either Kligler medium.

MAITLAND, A. I. L.: Severe hypertension with recovery after nephrectomy. (Brit. Med. J., March 12, 1949, 426-428).

The author describes a case of severe hypertension with advanced retinitis and papilledema in a young woman of 20. Headache, vomiting and diplopia suggested an intracranial lesion but G. U. examination revealed the left kidney as the probable cause of her disease. The removal of that organ with the left adrenal gland produced a return of the blood pressure to normal in half an hour, and a complete recovery from the retinal disease in a few weeks. This has been maintained now for 6 months. If such cases are to be detected, separate kidney function tests and Bilateral K. U. B. films are required. Perhaps not more than 8 similar cases have been reported. The adrenal gland was histologically normal but the removed kidney showed chronic pyelo-nephritis. The diseased kidney probably was producing a pressor substance, renin, due to its restricted blood supply. The author details several points which ought to be decided before doing a nephrectomy in such a case.

WOLD, L. E. and BAGGENSTOSS, A. H.: Gastro-intestinal lesions of periarteritis nodosa. (Proc. Staff Meet. Mayo Clinic, Jan. 19, 1949, Vol. 24, No. 2, 28-35).

Periarteritis nodosa is a rare disease, due perhaps, to an al-

lergic vascular reaction, in which blood vessels present focal inflammatory lesions in their walls. Arteries all over the body are affected. The lesions frequently lead to occlusion of the vessel and the production of infarcts in various organs. Diagnosis from clinical symptoms is difficult. 30 cases are presented, all of which had gastro-intestinal symptoms, the chief being abdominal pain, loss of weight and anorexia. Necropsy indicates mucosal congestion and marked petechial hemorrhages in the gut. In all the cases reported herewith, the periarthritis was confined to the arterioles of the submucosa. The parenchymal lesions consisted of hemorrhages and infarcts and the liver and jejunum were most affected. Peritonitis may occur from ulceration and perforation. Pain is usually caused by parenchymal lesions secondary to the vascular lesions. The nervous system is similarly liable to lesions and these may produce abdominal pain, by reference, when no intra-abdominal lesions are found to explain the pain.

BROWNING, E.: *Blood changes in luminizers using radioactive material.* (Brit. Med. J., Mar. 12, 1949, 428-431).

A "luminizer" is a person who is employed in the application of luminous compounds to any surface or the introduction of luminous compounds into glass tubing. A "luminous compound" means luminous material containing radioactive substance. Such persons were employed in large numbers during the war, and after the cessation of hostilities, the British government required that these persons have careful blood examinations for a number of years. Over a five year period there has been no evidence of bone marrow depression but rather a slight hyperstimulation, which is tentatively ascribed to an effect on the reticulo-endothelial system. Blood examinations after a period of one to four years following cessation of exposure show a complete disappearance of this hyperstimulative effect. Such an effect was evidenced at first by "high normal" total white counts with relative lymphocytosis, and the presence of abnormal cells which consisted chiefly of young forms of the large monocyte. The transient nature of these changes is supported by the results of direct gamma-ray estimation of the tissues and of estimation of radon in the exhaled air.

BIGNALL, J. R. AND CROFTON, J.: *Antihistamine drugs in treatment of nausea and vomiting due to streptomycin.* (Brit. Med. J., Jan. 1, 1949, 13-14).

In 17 of 49 cases being treated by streptomycin for tuberculosis, nausea and vomiting occurred, but this toxic symptom was severe in only 4 cases. In a well-controlled investigation of four patients, it was found that the symptoms were abolished or considerably reduced when benadryl capsules were given, but returned when the capsules were withheld. The "clue" to this therapy arose from the hypothesis that such toxic symptoms as urticaria were due to streptomycin or impurities in the products used and that nausea and vomiting might be caused in the same way and might therefore respond to antihistamine drugs. Giddiness caused by streptomycin was not relieved.

BRICK, I. B.: *Clinical significance of hiatus hernia.* (Miss. Valley Med. J., Jan. 1949, Vol. 71, No. 1, 2-8).

The condition of hiatus hernia has become recognized with increasing frequency in the past 20 years. During x-ray ex-

amination the Trendelenburg position ought to be used if the condition is not to be frequently missed. Among 3448 patients subjected to upper gastro-intestinal study, 308 or 8.93 per cent showed hiatus hernia. This was the second most frequent lesion diagnosed, duodenal ulcer having been found in 20.41 per cent. It increases in frequency up to middle-age, being commonest between 50 and 70. The condition may remain asymptomatic and be discovered by accident. The symptoms are most likely to be present in the smallest hernias. The symptomatic manifestations group themselves into syndromes which may simulate esophageal, gastric, duodenal, cholecystic and coronary disease, as well as gastrointestinal bleeding and anemia of undetermined origin. Chronic esophagitis is nearly always present and ulcer of the esophagus or benign stricture are not uncommon. Viscero-visceral reflex from a diseased gall bladder may precipitate or accentuate the symptoms of hernia. Substernal pain with radiation to the left shoulder and arm occurred in 28 per cent of a series, and mimics angina pectoris, especially since nitroglycerine relieves both pains. It is probable that the pain is actually an angina pectoris due to reflex spasm of the coronary arteries, from irritation of the lower end of the esophagus. Differentiation is made by the fact that hiatus hernia pain proper tends to disappear entirely for long periods, and by the electrocardiogram. Treatment should be medical,—bland diets with antacids and atropine, and acute symptoms controlled by nitroglycerine tablets. Large hernias with symptoms of obstruction should be treated surgically.

WILSON, C. H.: *Two unusual cases of disease of the alimentary canal.* (Med. J. Australia, Feb. 19, 1949, 234-236).

The first case was one of primary lymphosarcoma of the small intestine. Three distinct tumors were found at autopsy at various levels of the small gut. No diagnosis was possible before death and no operation was performed. Liver function was impaired, and the organ enlarged and there was an unexplained, massive ascites which made radiological examination very difficult. The author regards this case as "one of the more frequent of the rarities." The second case, confirmed at laparotomy, was a Friedlander bacillus intramural abscess of the stomach, which the author regards as unique, no other case having been reported in the literature. His symptoms combined with x-ray findings had suggested carcinoma of the hepatic flexure of the colon. Penicillin, sulfa drugs and streptomycin had no apparent effect on the disease. He apparently died of cardiac failure on the 13th post-operative day.

MARKS, J. L. AND NATHAN, A.: *The linear atelectatic sign in intra-abdominal lesions.* (Radiol. March 1949, Vol. 52, No. 3, 363-366).

A series of 26 cases of lineal atelectasis is presented. Although this series is small, the authors believe it to be significant because of the high incidence of associated intra-abdominal disease (80 per cent). In the past, diaphragmatic elevation has been utilized frequently as a sign of either an intrathoracic or intra-abdominal lesion. In many instances, the primary lesion has proved to be intrathoracic. The presence of lineal atelectasis, however, either with or without a high diaphragm, affords presumptive evidence of disease within the abdomen.

THREE VEE PAPAYA

Three Vee Papaya Meat Tenderizer is an extract of the tropical papaya melon, one of the few sources of papain. When applied to meats 5 minutes before cooking, it predigests (tenderizes) the meat, imitating the "ripening" of meat which occurs naturally through the agency of autolysins, but without alteration in the natural meat flavors or aromas. Marciano in 1891 prepared enzymatic digests of meat for the diet of invalids. Davisson in England recently produced a proteolyzed liver preparation of great value in treating certain cases of refractory pernicious anemia, utilizing papain as the active proteolytic agency. The Enzyme Research Laboratory of the U. S. Department of Agriculture determined several years ago that papain readily digests meat and liver. While Three Vee Papaya has been extensively used for the past ten years by the nation's leading chefs, only recently has it been offered, through physicians, for the use of invalids, the edentulous, and those recovering from exhausting illness. Physicians interested in this A. M. A.-accepted product may obtain complete details by writing to Mr. Martin Trasher, Frank Kierman and Co., 92 Liberty St., New York 6, N. Y.

WINTHROP-STEARN'S PARTICIPATES IN ARMED FORCES DAY

New York, N. Y.—Winthrop-Stearns, Inc., participated in Armed Forces Day, May 19, when firms honored during World War II flew their Army-Navy "E" flags, according to Dr. Theodore G. Klumpp, president.

Winthrop-Stearns, which was awarded the flag in 1942 with three subsequent additional citations in 1944, 1945 and 1946, displayed its awards in the company's main offices at 1450 Broadway, during the week beginning May 14.

Winthrop-Stearns supplied the armed forces in the last war with Atabrine, antimalarial; Pontocaine ointment for burns; salyrgan-theophylline, a mercurial diuretic; Diadrast, radiopaque substance; and other preparations.

Today, the firm supplies the armed forces in Korea with a num-

ber of products including Aralen, antimalarial which has replaced Atabrine. Aralen was first synthesized at the Sterling-Winthrop Research Institute, Rensselaer, N. Y.

SCHERING APPOINTS BOWLES HOSPITAL SUPERVISOR

Appointment of Mr. Robert Bowles as Central Division Hospital Supervisor has been announced by Dr. John N. McDonnell, vice-president of Schering Corporation, pharmaceutical manufacturers of Bloomfield New Jersey.

A graduate of the University of Nebraska, and a registered pharmacist in Nebraska and Minnesota, Mr. Bowles has had both chain and independent retail drug store experience. After service during World War II as a commissioned officer in the Marine Corps, he joined Schering in 1946 as a Professional Service Representative. More recently he has served in several capacities in Schering's home office. With headquarters in Chicago, he will be responsible for contacts with colleges of medicine and pharmacy, hospitals and research institutions in the Mid-West.

AMERICAN PUBLIC HEALTH ASSOCIATION, 1790 BROADWAY, NEW YORK, N. Y.

New York, N. Y., April 30.—The 79th Annual Meeting of the American Public Health Association, the 18th Annual Meeting of its Western Branch and the annual meetings of 38 related organizations will be held simultaneously in San Francisco, October 29 to November 2. The combined meetings, which will bring together 5,000 health specialists from all parts of the Western Hemisphere, were announced today by Dr. Reginald M. Atwater, Executive Secretary of the Association.

The protection and promotion of the nation's health is the obligation of professional public health workers, Dr. Atwater said, and they are keenly aware of their increased responsibility in the current emergency. In San Francisco, he said, they will hear more than 400 authorities discuss modern public health practice in all its aspects and

its vital relationship to national security and civilian defense.

No single theme can be utilized for a meeting of such scope, Dr. Atwater said. Symposia under development by the thirteen Sections of the Association which he named as Health Officers, Laboratory, Statistics, Engineering, Industrial Hygiene, Food and Nutrition, Maternal and Child Health, Public Health Education, Public Health Nursing, Epidemiology, School Health, Dental Health and Medical Care, are: Mobilization of the Nation's Health, International Health, Hygiene of Aging, Sanitary Aspects of the Food Supply in Time of Disaster, The Emergency Maternal and Infant Care Program—How to Do It This Time, Long Term Illness in Children, Biological Warfare, School Health Practices Today, Air Pollution, Food Faddism, Cancer Diagnostic Programs, Medical Care for the Needy, Industrial Sanitation, The Mental Health Institute as an Education Device, Chronic Diseases, Problems in Immunization, and Water Fluoridation.

Among the related organizations meeting with the Association are: American Association of Registration Executives, American Association of Schools of Public Health, Association of Maternal and Child Health and Crippled Children's Directors, Association of State and Territorial Health Officers, Commissioned Officers Association of the U. S. Public Health Service, Conference of Municipal Public Health Engineers, Conference of Professors of Preventive Medicine, Conference of Public Health Veterinarians, Conference of State and Provincial Public Health Laboratory Directors, Conference of State Directors of Public Health Education, Conference of State Hospital Personnel, Conference of State Sanitary Engineers, Council of State Directors of Public Health Nursing, Civil Affairs Committee of the Military Government Public Health Society, Public Health Cancer Association, and National Organization for Public Health Nursing.

Local arrangements are being made under the direction of Dr. J. C. Geiger, Director of Public Health of the City and County of San Francisco, Dr. Atwater said. Headquarters will be the Civic Auditorium.

ORETON-M BUCCAL TABLETS

Manufacturer: Schering Corporation, Bloomfield, New Jersey.

Active Constituent: Methyltestosterone U. S. P. in Polyhydrol, a unique solid solvent for steroid hormones.

Action: Oreton-M Buccal Tablets are made with an especially prepared Polyhydrol base, which permits absorption of methyltestosterone directly into the systemic circulation through the buccal and sublingual mucosae. By-passing the liver and the portal circulation, the active hormone is carried directly to the tissues. The considerably higher proportion of therapeutically available active hormone compares favorably with an injection of testosterone propionate.

Indications: Oreton-M Buccal Tablets are indicated in androgen deficiencies, such as *prepubertal hypogonadism* or *eunuchoidism*, and the *male climacteric* or *functional hypogonadism of middle age*.

Dosage: After initial standardization of the patient by means of Oreton injections, patients may be maintained on one-half to one 10 mg. Oreton-M Buccal Tablet daily. In some cases, one-half an Oreton-M Buccal Tablet three times weekly will be sufficient.

Administration: The tablet is placed well into the lower buccal space adjacent to the buccal surface of the gums, opposite the first molar tooth. The tablet is absorbed in 30 to 60 minutes. The patient may talk or swallow *ad libitum*. Tablets do not stimulate salivation. Mid-morning, mid-afternoon and before retiring are the best times for administration of the medication.

Packaging: Oreton-M Buccal Tablets are available in 10 mg. strengths, bottles of 30 and 100 tablets.

LARGER CREAMALIN PACKING AT SAME PRICE MADE FOR HOSPITALS

New York, N. Y.—Winthrop-Stearns Inc. has introduced at no increase in price a new packing for Creamalin and Tricreamalate liquid, designed for hospital use.

The new 8-ounce blue bottle re-

places the flint 6 ounce bottle previously used in hospital units of the two products. The units, of 36 bottles, remain the same.

Creamalin and Tricreamalate are aluminum hydroxide gels, the latter containing magnesium trisilicate in addition. The preparations are described as nonabsorbable, nonalkaline antacids, used for the treatment of peptic ulcers and gastric hyperacidity.

AMES COMPANY

Ames Company, Inc., of Elkhart, Indiana, has announced through its President, Charles F. Miles, the appointment of George W. Orr, Jr., as Vice-President in Charge of Sales. Mr. Orr's appointment is another step in the sales expansion program of Ames Company, Inc.

Mr. Orr has been serving the Wm. S. Merrell Company of Cincinnati, Ohio, in the capacity of General Sales Manager and member of the Board of Directors. Before his appointment as General Sales Manager he held the positions of Advertising Manager, Assistant to the President and Assistant to the General Sales Manager. Prior to joining Merrell he served three years with the Vick Chemical Company in New York City.

Mr. Orr is a graduate of Duke University; is married and has one daughter. He will assume his duties with Ames Company, Inc. on May 1st.

CANCO APPOINTS GENERAL MANAGER OF MANUFACTURE

G. W. Reese, associated with the American Can Company for 31 years, has been appointed general manager of manufacture, it was announced by W. C. Stolk, president.

Formerly assistant general manager of manufacture, Mr. Reese succeeds S. D. Arms, who recently was elected vice-president in charge of the company's Atlantic division.

At the same time Mr. Stolk announced the appointment of four other men to important manufacturing posts opened by recent promotions.

F. J. Green and C. F. Lausten, formerly managers of manufacture

in the firm's Atlantic and Pacific divisions respectively, have been named assistant general managers of manufacture. Mr. Green has served the company for 28 years and Mr. Lausten for 23 years. In their new posts, they succeed R. F. Hepenstal, who recently was elected vice-president in charge of manufacture, and Mr. Reese.

R. B. Thompson and A. T. Augensen, formerly assistant managers of manufacture in the Atlantic and Pacific divisions respectively, have been promoted to managers of manufacture of the divisions in which they held their previous positions. Mr. Thompson has been associated with Canco for 29 years and Mr. Augensen for 34 years.

COMMERCIAL SOLVENTS ANTIBIOTICS AWARD WON BY TERRAMYCIN RESEARCH GROUP

Chicago, May 29.—The 1950 Commercial Solvents Award in Antibiotics was presented tonight at the annual meeting of the Society of American Bacteriologists to the Terramycin Research Team of the Chas. Pfizer & Co., Inc. The Award, which consists of a gold medal and \$1,000, was presented by Dr. Walter J. Nungester, President of the Society, to Dr. G. L. Hobby who was designated spokesman for the research group.

The award committee, composed of members of the Society, selected the Pfizer group for the discovery of the new antibiotic, Terramycin. Studies included the isolation and crystallization of the active material, its chemical and physical characterization, and the determination of its toxicity and antibacterial activity.

Members of the research group, who also received individual scrolls, included A. C. Finlay, Dr. G. L. Hobby, J. H. Kane, Dr. S. Y. P'an, Dr. P. P. Regna, Dr. J. B. Routien, Dr. D. B. Seeley, Dr. G. M. Shull, Dr. B. A. Sobin, I. A. Solomons, and J. W. Vinson.

The Commercial Solvents Award was established in 1950 and is administered by the Society of American Bacteriologists. It is awarded to any person or group of persons working in the Western Hemisphere who have contributed outstanding work in the field of antibiotics during the past year.

NEW CODEINE DERIVATIVE FORMULATED BY ENDO PRODUCTS

To meet the needs of an analgesic stronger than codeine, but less potent than morphine, Endo Products, Inc., is introducing dihydrohydroxycodone, a new codeine derivative. This will be marketed in two different forms under the brand names Percodan and Nucodan. Both compounds are administered orally and may be used interchangeably. They require a dose of only 1/4 to 1/5 of codeine to achieve the same effect. The action of both Percodan and Nucodan is more rapid than that of codeine, the effect is more prolonged and there is less likelihood of untoward reactions. They are recommended for use in all types of moderate pain.

Each Percodan tablet contains:

Dihydrohydroxycodone hydrochloride, 4.50 mg.

Dihydrohydroxycodone terephthalate, 0.38 mg.

Homatropine terephthalate, 0.38 mg.

Acetylsalicylic acid, 224 mg.

Acetophenetidin, 160 mg.

Caffeine, 32 mg.

Each Nucodan tablet contains:

Dihydrohydroxycodone hydrochloride, 4.50 mg.

Dihydrohydroxycodone terephthalate, 0.38 mg.

Homatropine terephthalate, 0.38 mg.

Pentylentetrazol, 50 mg.

Percodan is especially indicated in all cases of acute pain, Nucodan in chronic conditions or in cases of heart and respiratory disease. Nucodan contains pentylentetrazol, an antidote for opium derivatives, which counteracts certain undesirable effects of opiates. Both Percodan and Nucodan tablets are supplied in bottles of 100, 500 and 1000 scored tablets, on prescription.

suspension containing 50 mg. of pure minute crystals per cc.

Action: Laboratory and clinical reports indicate that Methostan, a steroid chemically closely related to methyltestosterone, will provide beneficial protein anabolic effects without the undesired androgenic action sometimes resulting from the use of testosterone. In castrate rats, only slight effect is noted upon the prostate and seminal vesicles. In humans, 17-ketosteroid excretion is not influenced significantly. Masculinizing symptoms did not appear in female patients receiving 100 mg. daily for several weeks. Studies indicate high renotropic action of Methostan. Creatinine excretion is increased, and total blood protein elevated. A positive nitrogen balance is achieved.

Indications: Indicated in retarded growth and constitutional diseases accompanied by protein wastage when such conditions do not respond to diet or to more specific therapy. According to Cantarow and Trumper, negative nitrogen balances are commonly found when protein, carbohydrate or total caloric intake is less than is required under existing conditions, such as may occur in conditions accompanied by vomiting, diarrhea, fever or wasting (typhoid, tuberculosis, malaria, pneumonia, septicemia of bacteremia, malignancy, leukemia, diabetes mellitus), dehydration, excessive diuresis or purgation, hyperthyroidism, pituitary basophilism, adrenal cortical hyperfunction, intestinal obstruction, and burns.

Dosage: Adults: 10 to 40 mg. daily, with either dosage form. Children: 5 to 10 mg. daily or less frequently until susceptibility to androgenic effects has been ruled out.

Packaging: Aqueous suspension: Vials of 10 cc., boxes of 1 and 6 vials. Tablets: Bottles of 30 and 100.

reduced dosage for children or adults may be given where indicated.

Effective April 9, the smaller 0.25 gram tablet has been discontinued.

With the larger tablet, dosage for treatment of amebiasis is one tablet three times a day for seven days. With the smaller tablet, the usual adult dosage was two tablets taken three times a day for seven days.

The incidence of amebiasis in the general population of the United States has been estimated at from ten to twenty per cent. Milibis has proven effective in single course treatment in a high percentage of these cases, although on occasion, persistent, positive stool findings have indicated supplementary therapy.

The new Milibis tablets, being distributed nationally, come in bottles of twenty-five.

SKLAR

A new compact and mobile Sklar Electric Evacuator, designed for Wangenstein technique, has been announced by the J. Sklar Manufacturing Company of Long Island City, N. Y., and will be distributed through accredited surgical supply houses.

Features of the new unit, perfected after several years of research, include an intermittent "on and off" pilot light, affording constant visual performance check; an automatically ventilated motor unit, and minute control over the range of suction and pressure. Suction is calibrated from 50 to 250 cm. of water.

The stand is mounted on casters, and a Sklar ivory-baked enamel finish gives the unit an attractive appearance. It is noiseless and vibrationless in operation and has been found to perform efficiently during prolonged and continuous use.

No maintenance or lubrication are required, and the unit carries a two-year guarantee. Equipment includes a gallon-size suction bottle, a 32-ounce irrigating bottle and a trap bottle.

Listed as No. 100-160 Sklar Electric Evacuator, 110-120 Volt, 60 Cycle AC, Complete on Stand, the unit is designed to meet the many and variable clinical requirements for controlled low-grade suction and pressure in preoperative and postoperative procedures.

AMER. JOUR. DIG. DIS.

NEW PRODUCT

METHOSAN — Tablets and Aqueous Suspension

Manufacturer: Schering Corporation, Bloomfield, New Jersey.

Active Constituents: Methostan, brand of methandriol (methyl-androstenediol, 17 alpha-methyl-delta-5-androstene-3 beta, 17 beta-diol); in 25 mg. tablets, and in aqueous

LARGER MILIBIS TABLETS INTRODUCED

To facilitate administration by reducing the number of tablets required in the treatment of amebiasis, Winthrop-Stearns Inc. has introduced Milibis tablets in a new 0.5 gram size, it was announced by Joseph C. Noh, vice-president and director of sales. The new 0.5 gram tablet has been scored so that



Are your gallbladder patients tired of a fat-free diet?



OXSORBIL* Capsules are specifically formulated for the large number of such patients. Besides time-proven ingredients to promote the flow of bile and assist in the evacuation of a static gallbladder OXSORBIL Capsules contain a new enormously efficient non-toxic fat emulsifier!..

SORBITAN MONOOLEATE POLYOXYETHYLENE DERIVATIVE.

This fat-emulsifier permits the inclusion of larger quantities of suitable (dairy and vegetable) fats—for their highly desirable physiologic chologenic action . . . and also to improve the patient's nutrition.

The administration of OXSORBIL Capsules thus speeds the return to a more normal diet and facilitates the physiological rehabilitation of gallbladder patients.

INDICATIONS: In Chronic Cholecystitis, Non-calculous Cholangitis, Post-cholecystectomy Syndrome, Biliary Dyskinesia, Biliary Stasis without Total Obstruction.

FORMULA: Each Oxsorbil Capsule contains:
 Dehydrocholic Acid ½ grain
 Desoxycholic Acid ½ grain
 Extract of Ox Bile, U.S.P. 1 grain
 Sorbitan Monooleate Polyoxyethylene
 Derivative 2½ grains
 Oleic Acid, U.S.P. 2¾ grains

DOSAGE: One to two capsules three times a day or as directed by the physician.

SUPPLY: In bottles of 100 capsules.

REF.: 1) Jones, C. M., et al.: Ann. Int. Med. 29:1-10, July 1948
 2) Becker, G. H., et al.: Gastroenterology 14:80-91, Jan. 1950

If you would like to receive copies of our gallbladder diet sheets for use with Oxsorbil Capsules, clip and mail this coupon:

Please send me gallbladder diet sheets.

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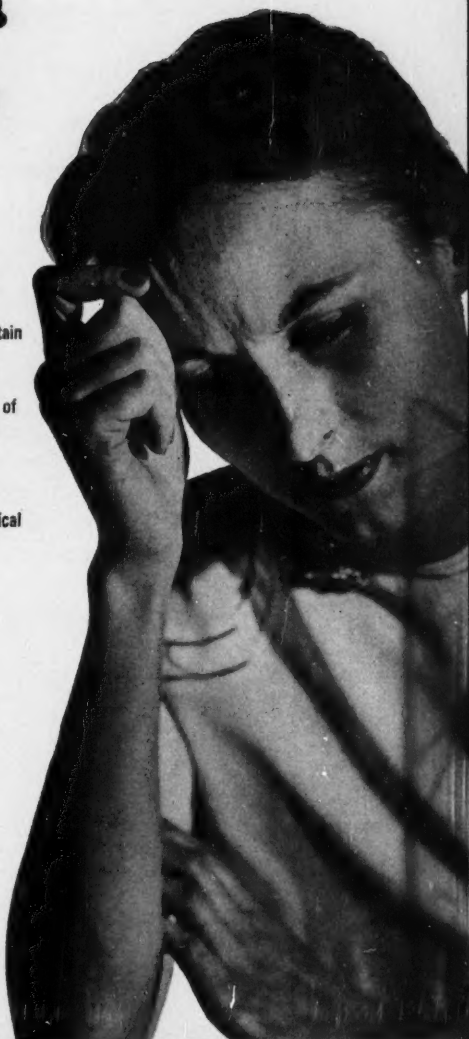
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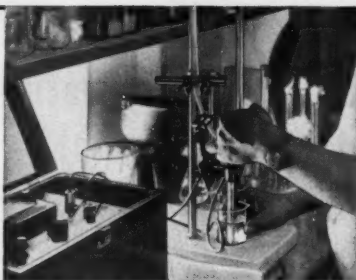
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Supported by Clinical Evidence . . . Combined oral sulfonamide-penicillin therapy gave striking therapeutic results in pneumonia, indicating a synergistic effect.²

1. Bigger, J. W.: *Lancet* 2:46, 1950.

2. Volmer, H., Pomerance, H. H., and Brandt, I. K.: *New York State J. Med.* 50:2293, 1950.

Powerful double-barrelled weapon against infection

- Synergism of two potent antibacterial agents.
- Sustained effectiveness because of overlapping absorption rates.
- Simplicity and convenience of oral therapy.

150,000 units crystalline potassium penicillin-G and 0.5 Gm. total sulfonamides (0.166 Gm. each of sulfadiazine, sulfamerazine, and sulfamethazine) in each tablet.

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CLINICAL EFFECT
OF
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Turicum provides lubricoid softness *without oil*—an ideal which has been the therapeutic aim in constipation management for decades.

The unique lubricoid action of Turicum is based on the administration as the active ingredient of methylcellulose, with magnesium hydroxide in less than laxative dosage to maintain continued hydration within the bowel.

In constipation the hydrophilic lubricoid mixes with and softens the fecal content, permitting easy elimination without stimulation.

Turicum is easy to take—palatable, non-bloating—does not interfere with absorption of oil-soluble vitamins. Average dose: One or two tablespoons at bedtime, followed by a full glass of water.

Turicum is available in one pint bottles.

N. F. I. P.

The National Foundation for Infantile Paralysis announces a new type of short-term predoctoral fellowships for undergraduate medical students who are interested in research in medicine and the related biological and physical sciences. The fellowships cover a minimum of two months experience in research under the direction of a competent investigator in the laboratories of approved medical schools or research institutes in the United States.

Under the plan, the Dean of each four-year medical school has the privilege of nominating one medical student to receive a fellowship. The National Foundation for Infantile Paralysis will provide a stipend of \$400 for each student who qualifies for the summer laboratory study.

The new fellowships, as well as the regular pre and postdoctoral fellowships currently being offered by the National Foundation, are administered by its Division of Professional Education with the assistance of a professional committee headed by Dr. Thomas B. Turner, Professor of Bacteriology at the School of Hygiene and Public Health of Johns Hopkins University.

The purpose of the new short-term fellowships is to enable medical school students to test their desires and determine their aptitudes to participate in research in medicine and related biological sciences at an early stage in their professional careers.

SCHERING AWARD WINNERS ANNOUNCED

Dr. S. I. Griboff of New York, serving his internship at New York City's Mt. Sinai Hospital, has been announced as the winner of "The Schering Award for 1950." Dr. Griboff was a senior medical student at Syracuse University College of Medicine when he enrolled in the competition. Mr. Francis C. Brown, president of Schering Corporation, presented the check for the first prize of \$1000. to Dr. Griboff for his paper on "The Clinical Use of Steroid Hormones in Cancer." The ceremony took place in the executive offices of Schering, pharmaceutical manufacturers in Bloomfield, New Jersey, in the presence of

Dr. John N. McDonnell, vice-president, Dr. Norman L. Heminway, Associate Director of Clinical Research; and Dr. George Babcock, Jr., chairman of the Schering Award Committee.

Co-authors Robert W. Winters and Henry M. Williams, both third year students at Yale University School of Medicine, New Haven, Connecticut, were selected as a tie for second prize by the judges with Kenneth J. Ryan, third year student at the Boston's Harvard Medical School. They were awarded duplicate prizes of \$500. each. Monte J. Meldman, third year student at Marquette University School of Medicine, Milwaukee, Wisconsin, was awarded the third prize of \$300. Twenty-five contestants received honorable mention, and each received special awards in acknowledgement of their contributions.

"The Schering Award" has been given annually for many years for the best manuscripts prepared on designated phases of endocrinology. Medical students of the United States and Canada are eligible for the contest. The majority of medical schools are represented by applicants.

Each year three physicians prominent in the clinical field covered by the subject act as judges for "The Schering Award" competition. The judges for the 1950 Award were Dr. Ira T. Nathanson, Assistant Professor of Surgery, Harvard Medical School; Dr. Cornelius P. Rhoads, Director of the Memorial Center for Cancer and Allied Diseases, New York City; and Dr. Walton W. Van Winkle, former Secretary of the Committee on Research of the Council on Pharmacy and Chemistry of the American Medical Association.

INSTITUTE MEN DISPLAY RADIOPAQUES, SHOW NEW TECHNIQUES, AT CONFERENCE

Cleveland, O.—Current developments in radiopaque substances, including a new preparation for visualization of the gall bladder region and several techniques for the study of such substances, were demonstrated by scientists from the Sterling-Winthrop Research Institute, Rensselaer, N. Y., at the annual meeting

of the Federation of American Societies for Experimental Biology, held in the Auditorium here.

The new radiopaque substance, developed after several years of research, was the highlight of an exhibit on techniques in the study of radiopaques useful in myelography, X-ray of the spinal canal; cholecystography, X-ray of the gall bladder; and urography, X-ray of the kidneys.

Dr. James O. Hoppe, of the Institute's pharmacology laboratories, presented an exhibit illustrating a technique he has developed for judging cholecystographic agents by means of an X-ray photograph grading system. He also demonstrated the plotting of a dose-response curve, important in the field of radiopaques.

Dr. Maurice C. Olivier, also of the pharmacology section, discussed recent developments in vascular physiology; and Dr. Jesse I. Grant read a paper on the synergistic action of new bronchodilator agents with antihistaminic drugs.

Among those from the Institute attending were: Dr. E. W. Dennis, director of the biological sciences division; Dr. John C. Seed, executive assistant to the director of the Institute; John Hart, director, new products division; and Dr. Oliver H. Buchanan, secretary of the Institute.

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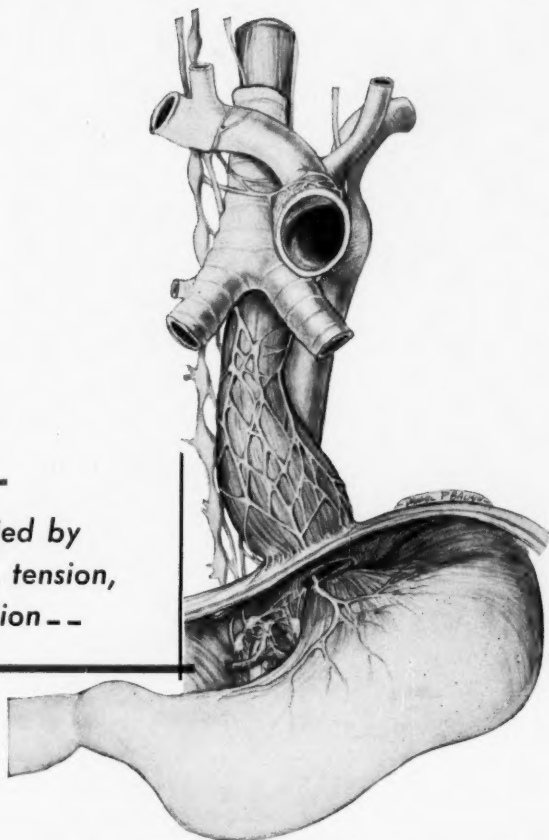
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Pavatrine is unique in that it exerts two types of spasmolysis—neurotropic and musculotropic—for relief of gastric hypermotil-

ity, cardiospasm, pylorospasm, spasticity of the duodenum including the sphincter of Oddi, bladder spasm and dysmenorrhea.

For the medical management of gallbladder disease, Pavatrine with Phenobarbital is useful in conjunction with the hydrocholeretic, Ketochol.

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